The Patent Economics of Synthetic Biology

– A European framework for optimal SynBio innovation

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Tiivistelmä/Referat – Abstract

The work in question seeks to set a relatively novel form of biotechnology, synthetic biology, in the frame of European intellectual property law, with an additional focus on patent law. The primary questions that the thesis seeks to address are 1) is synthetic biology structurally incompatible with existing forms of patent law, and 2) if some incompatibility is evident, what measures are best suited to ameliorate it. Methodologically, the thesis is heavily oriented towards a combination of legal dogmatics for descriptive sections and a classical law & economics approach for the normative sections.

The specific form of synthetic biology discussed in the thesis is the so-called biopart-approach (also known as biobricks), which seeks to standardize DNA and other cellular material into modular units, which can subsequently be constructed into devices and systems, implemented in a minimal genome chassis, resulting in a synthetically constructed organism. Such organisms may exhibit properties which are more commonly associated with e.g. computers. The fundamental difference between synthetic biology and other forms of genetic engineering is the introduction of true engineering principles, mathematical modelling, standardization, quality characterization, and modular construction. The research community involved in synthetic biology exhibits two distinct forms of IP practices: the IP frame is a continuation of pre-existing practises in biotechnology, in which innovations are typically appropriated through patenting. The A2K frame seeks to limit the role of IP concerns in the development of synthetic biology, somewhat analogous to how the computer operating systems market is divided into proprietary actors and open source advocates. It is taken as a matter of course that the A2K frame will not exhibit major issues in innovation being hindered from within their own group. However, the same cannot be said in regards to the IP frame.

The bioparts, devices, systems and chassis, along with all of their requisite enabling technologies, biotechnological standards, and research tools are patentable subject-matter as defined in the Biotechnology Directive and EPC. One section of the thesis is devoted to exploring the implications of both EU and EPO jurisprudence on the patenting of synthetic biology. The main focus of the latter part of the work concentrates on the fact that many of the aforementioned elements of the bioparts approach are complementary goods. This raises a problem when they are granted in a disaggregated manner, as licensees must conduct a series of non-coordinated negotiations with multiple patent holders to obtain the upstream patents needed for the development of downstream commercial applications. This fragmentation of exclusionary rights is called an anticommons. Furthermore, patent claims may not be entirely independent, with the production of a seemingly discrete technology requiring the licensing of multiple overlapping input patents. This configuration is called a patent thicket. Given the international nature of synthetic biology research, and the ever increasing strain on patent offices and its concomitant effect on patent quality, it is possible that synthetic biology will exhibit both phenomena. Despite the difference in origin, these phenomena result in a similar series of market failure, namely a) royalty stacking, b) patent hold-up, and c) suboptimal transaction costs in the form of high bargaining costs and search costs. These problems exacerbate each other, and they tend to exhibit a somewhat monotonic relationship with increased patenting. Both anticommons and patent thickets are well-known and studied in relation to e.g. the ICT and semiconductor industries.

The last section of the thesis explores various options to resolve both the anticommons and patent thicket. The options are divided into market solutions, such as cross-licensing, patent pooling and patent clearinghouses, as well as patent policy tools, such as patent quality management, public institution participation in the IP market and the role of courts as potential arbiters of innovation and utility. An underlying theme in the work is the presumed advent of the unitary patent system, as well as its accompanying Unified Patent Court, and their effects on the incentive structures of actors within the IP frame.

Avainsanat – Nyckelord – Keywords
synthetic biology; biotechnology; intellectual property law; patent law; patent economics; anticommons; patent thicket

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Tiivistelmä/Referat – Abstract

Kyseinen työ tutkii uutta bioteknologian muotoa, synteettistä biologiaa, ja sen suhdetta eurooppalaiseen immateriaalioikeuteen, erityisesti patenttioikeuteen. Tutkielman keskeiset kysymykset koskevat sen selvittämisestä, onko 1) synteettisen biologian keksinnöt systeemisesti soveltumattomia nykyiseen patenttioikeuteen, ja 2) mikäli näin on, mitä asialle tulisi tehdä. Metodologisesti työ on yhdistelmä lainoppia ja oikeustaloustiedettä. Lainopin rooli tutkimuksessa on deskriptiivinen, kun taas oikeustaloustiede toimii normatiivisen argumentaation lähteenä.

Tutkielma keskittyy ns. bioparts-menetelmään, jossa DNAta ja muita biologisia materiaaleja pyritään standardoimaan ja modularisoimaan siten, että niistä on mahdollista rakentaa biolaitteita (devices) ja biojärjestelmiä (systems). Kyseiset järjestelmät puolestaan implementoidaan alustaan (chassis), kuten miminaaligenomin omaavaan e. coli-bakteeriin, jonka seurauksena on synteettisesti rakennettu ja suunniteltu eliö, jonka toiminta voi muistuttaa enemmän esimerkiksi tietokonetta kuin tavallista bakteeria. Synteettisen biologian keskeinen ero aiempaan bioteknologiaan on sen pyrkimys omaksua insinöörillisiä perusperiaatteita, kuten matemaattisia mallinnusmekanismeja, standardisaatiota, komponenttien karakterisaatiota ja modulaarisia rakennusperiaatteita.

Itse synteettisen biologian tutkijat ovat jakaantuneet kahteen leiriin heidän immateriaalioikeudellisen suhtautumisen perusteella. Yhtäällä osa alan toimijoista kannattaa bioteknologiasta omaksuttuja käytäntöjä, joissa patenteilla on keskeinen rooli, toisaalta on puolestaan open source-mallin omaksuneet tutkijat, jotka pyrkivät jakamaan tietoa mahdollisimman vapaasti ja estämään immateriaalioikeuksien haitallisia vaikutuksia tutkimustyössä. Tutkielman oletusarvona on se, että open source-mallin toimijat eivät tule itse aiheuttaneeksi heikennyksiä innovaatiotoimintaan, mutta immateriaalioikeusmallin kannattajien toimien vaikutukset voivat kattaa molemmat ryhmät

Bio-osat, laitteet, järjestelmät ja alustat ovat kaikki potentiaalisesti patentin arvoisia keksintöjä. Lisäksi synteettisen biologian primääriteknologiat, biotekniset standardit ja tutkimusvälineet ovat yhtä lailla patentoitavissa Bioteknologiadirektiivin ja Euroopan patenttisopimuksen mukaisesti. Tästä syystä yksi työn osio keskittyy tutkimaan Euroopan unionin ja Euroopan patenttitoimiston oikeiskäytäntöä, mitä kautta on mahdollista hahmottaa tulkintoja, joilla on vaikutuksia synteettisen biologian kehittämisprosessissa. Työn loppuosio rakentuu sen ajatuksen varaan, että monet em. keksinnöistä ovat komplementaarisia. Tästä voi aiheutua merkittäviä ongelmia jos ja kun patenttioikeuksia myönnetään sirpaloidusti, sillä käyttöluvan hakijan tulee solmia useita eri epäkoordinoituja lisenssisopimuksia useiden eri patentinhaltijoiden kanssa. Tilanne on erityisen haitallinen silloin, kun em. patentit ovat välttämättömiä uuden keksinnön kehittämisessä (ns. upstream-patentit). Fragmentaation seurauksena on ns. anticommons, joka suomeksi käännettynä lienee ”anti-yhteismaan ongelma”. Lisäksi upstream-patentit voivat olla jossain määrin päällekkäisiä, jolloin käyttöluvan hakijan tulee myös solmia useita lisenssisopimuksia usean eri patentinhaltijan kanssa. Tätä ilmiötä kutsutaan patent thicket:iksi, jonka suomennos lienee patenttiryteikkö. Molemman ilmiön seuraukset ovat pitkälti samankaltaisia, nimittäin a) lisenssimaksujen kasautuminen, b) patent hold-up ja c) epäoptimaalinen transaktiokustannusrakenne, erityisesti etsintä- ja neuvottelukustannusten osalta. Sekä anticommons-ilmiö että patenttiryteikkö ovat hyvin tunnettuja taloustieteellisiä ilmiöitä, sillä niitä on esiintynyt mm. tietotekniikan alalla runsaasti.

Tutkielman viimeinen osuus esittää eri metodeja em. ongelmien selvittämiseen, joista yksi osa koostuu markkinaperusteisista ratkaisuista, kuten ristilisensoinnista, patent pool:eista ja patenttiselvitystoimistoista. Toinen osio koostuu enemmän patenttiviranomaisten omista linjanvedoista, erityisesti liittyen myönnettyjen patenttien laadunhallintaan, julkisyhteisöjen osallistumisesta synteettisen biologian kehitystoimintaan ja tuomioistuinten rooliin mahdollisten tehokkuushyötyjen tuojina. Koko tutkielman yhdistävänä teemana tältä osin on yhtenäispatenttijärjestelmän voimaantulo ja sen mahdolliset vaikutukset synteettisen biologian toimijoiden insentiivirakenteisiin.

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Abbreviations

A2K	Access to Knowledge
cDNA	Complementary DNA
DNA	Deoxiribonucleic Acid
EBA	EPO Enlarged Board of Appeal
ECJ	Court of Justice of the European Union
EPC	European Patent Convention
EPO	European Patent Office
ESAB	EPO Economic and Science Advisory Board
EU	European Union
FRAND	Fair, reasonable and non-discriminatory
iGEM	international Genetically Engineered Machine competition
IP(R)	Intellectual property (rights)
JCVI	J. Craig Venter Institute
OECD	The Organization for Economic Co-operation and Development
rDNA	Recombinant DNA
RRI	Responsible Research and Innovation
SBPR	Registry of Standard Biological Parts
SCOTUS	Supreme Court of the United States
SynBio	Synthetic biology
TBA	EPO Technical Board of Appeal
TRIPS	Agreement on Trade-Related Aspects of Intellectual Property Rights
TTA	Technology Transfer Agreement
TTBER	Technology Transfer Block Exemption Regulation
UM	Utility Model
UPC(A)	Unified Patent Court (Agreement)
WIPO	World Intellectual Property Office
WHO	World Health Organization

1. Introduction

1.1. Regio: Synthetica

"WHAT I CANNOT CREATE, I CANNOT UNDERSTAND" – Richard Feynman

– Quote encoded in the genome of the synthetic *Mycoplasma laboratorium* by researchers at the J. Craig Venter Institute[1]

Since the discovery of DNA by Watson and Crick in 1953, our relationship with nature has undergone a fundamental shift. Instead of being purely at the mercy of our evolutionary past, we humans have sought to modify the underlying structures of life to better suit our needs. The second major milestone in this endeavor was the development of recombinant DNA (rDNA) technology in 1973 by Cohen and Boyer, which allowed the introduction of strands of DNA from one species to another.[2][3] Pioneering rDNA researchers were confident in the prospects of the new discipline, imagining a future in which life could be completely redesigned from the ground up, or in the words of Polish oncologist Wacław Szybalski, one that allows us to build a "new better mouse"[4]. It seemed that the advent of an era of synthetic organisms, the likes of which have never existed in nature, was imminent.

Recombinant DNA and other related fields of biotechnology have undoubtedly thrived scientifically and economically in the intervening years: the global biotechnology industry was worth an estimated 216.5 billion US dollars in 2011, with a projected value of 414.5 billion USD by the end of 2017[5], rising to 775.2 billion USD in 2024[6]. However, rDNA technology did not quite live up to the expectations of Szybalski and others. This changed in the late 1990s, when, among others[7], a graduate student by the name of Timothy S. Gardner was pondering how to recreate Luke Skywalker's bionic arm from the movie Star Wars.[8] His insight was to view the issue not only in terms of genetic engineering or molecular biology, but to add notions from fields such as electronic engineering and

[1] JCVI Press release 2010, paragraph 12.
[2] Glick et al. 2010, p. 5.
[3] *N.B.:* Other major milestones of discovery include those of the polymerase chain reaction (PCR) in 1983, and the completion of the sequencing of the human genome in 2003.
[4] Szybalski 1974, p. 405.
[5] PRNewswire Summary 2014.
[6] GlobeNewswire Summary 2016.
[7] Other commonly cited pioneers of the field include Drew Endy, Tom Knight and J. Craig Venter.
[8] Gardner & Hawkings 2013, p. 871.

computer science.[9] This idle notion resulted in serious research efforts, culminating in a 2000 article published in the prestigious journal Nature. In the article, Gardner describes how he and other researches had developed a genetic toggle switch.[10] If networked together, these switches could be used to create programmable and self-contained cellular memory circuits that enable the control of cellular functions[11], broadly similar in concept to how an assemblage of transistors operates in a computer. This and other similar innovations generated a good deal of media attention at the time[12], helping to breathe life to Szybalski's idea of synthetic organisms. Bearing in mind Gardner's combination of different scientific traditions, this new form of synthetic biology differed from its previous iteration by focusing on "reusable biological parts, predictive mathematical design and simulation of the circuit properties and elements of programmable digital logic"[13].

The ever increasing value of the biotechnology industry coupled with the cutting-edge nature of the research involved, as exemplified by synthetic biology, has put a strain on our existing legal systems in more ways than one. One major instance of such strain has been in the field of intellectual property rights (IPRs). Questions relating to the proprietary nature of biotechnological innovation in general have sparked controversy, leading to ongoing bioethical debate on what can and should be patentable.[14] The legal side of this debate has centered on issues such as the patentability of organisms created by the use of recombinant DNA technologies[15], as well as the intellectual property rights of genetic sequences found in nature[16]. Building on the advances of existing forms of biotechnology, synthetic biology is at least in part a subject of this ongoing debate. However, synthetic biology may potentially expand our mastery of biological systems in entirely new ways, which in turn have the potential to generate new and problematic IP scenarios. As such, it is hardly surprising that intellectual property dimension of synthetic biology has generated a substantial amount of academic interest among lawyers, economists and even synthetic biologists themselves.

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[9] *Idem.* p. 671.
[10] Gardner et al. 2000, *passim.*
[11] *Idem.* p. 342.
[12] See *e.g.*: Eisenberg 2000, *passim.*
[13] Gardner & Hawkins 2013, p. 871.
[14] For a summary of the main points of this debate, see e.g.: Stazi 2015, p. 49–56.
[15] See *e.g.*: EPO Technical Board of Appeal decisions T 0019/90 (Onco-mouse) and T 0315/03 (Transgenic animals/HARVARD)
[16] See *e.g.*: the US Supreme Court decision *Association for Molecular Pathology v. Myriad Genetics*, No. 12-398 (569 U.S. ___ June 13, 2013) and the EPO case T 1213/05 (Breast and ovarian cancer/UNIVERSITY OF UTAH), both revolving around the patenting of the naturally occurring BRCA1 and 2 genes.

Many national and intergovernmental institutions have begun to consider the challenges posed by the maturation of synthetic biology. In 2014, the OECD published an extensive multidisciplinary report on the subject, with a segment devoted specifically to IP policy considerations.[17] The European Union has had its own discussion on the topic, culminating in 2014–2015 with the publishing of three opinions that consider 1) the definition of synthetic biology[18], 2) risk assessment and safety aspects[19], 3) possible environmental risks and research priorities in the field[20]. IPR-related issues are only briefly mentioned, albeit highlighting the challenges the technology may pose to the existing IPR paradigm.[21] On a national level, the Finnish Academy of Sciences has its own multidisciplinary program, FinSynBio, which began in 2013 and is set to conclude in 2017. This program includes a research goal of studying the IP aspects of synthetic biology.[22] However, this goal did not result in any grants being given to researchers[23], which leads to the tenuous conclusion that this avenue of research is currently not being pursued at all within the FinSynBio program.

It is hardly surprising that synthetic biology has garnered such levels of interest. The technology has the potential to solve or at least assist in solving many of the greatest challenges faced by our modern societies, such as the production of renewable sources of energy[24] or affordable medicaments[25] to name but two. In economic terms, it has the potential to improve *total welfare.*[26] Therefore it is imperative to ensure SynBio is given the opportunity to address these issues, which in turn requires a systemic approach that ensures its economic viability as a technology. This is the primary objective of this thesis, consequently setting it in the "pragmatist-efficient" position of biotechnological patent theory.[27] Attaining this objective requires an understanding of the effects of our current European IPR systems, both in legislation and in practice, on that viability. If the effects are negative, i.e. such that they reduce the viability of the technology, it is necessary to amend those systems. For reasons that will be explained shortly, this thesis will focus on the patent system.

[17] OECD SynBio Report 2014, p. 93–115
[18] Opinion on Synthetic Biology I.
[19] Opinion on Synthetic Biology II.
[20] Opinion on Synthetic Biology III.
[21] Opinion on Synthetic Biology I, p. 54.
[22] FinSynBio Ohjelmamuistio, 3.3., p. 4.
[23] FinSynBio Ohjelmaesite, Rahoitettavat hankkeet, p. 5.
[24] Selgelid & Evans 2015, p. 8.
[25] Weber & Fussenegger 2012, 25.
[26] See *e.g.*: Motta 2004, p. 18–22 for a definition of this concept.
[27] See *e.g.*: Stazi 2015, p. 50–52 for a description of this theoretical position, as well as opposing views.

1.2. Regulating emerging technologies

It is not always certain how authorities should adapt their legislative and regulatory systems to take into account the issues raised by such novel technologies as synthetic biology. It can be argued that as the developmental pace of new technologies increases, it is often so that the previous framework of governance is in some way unsuitable to the new technological state of affairs, requiring constant legislative changes to adapt to the new situation. Marchant refers to this as the *pacing problem*, which he argues is a result of a static view of society and technology instead of a dynamic one, leading to the diminished capability of legal institutions, such as the legislature, regulators and courts, to adjust to new challenges.[28] If improperly managed, the mismatch caused by the pacing problem may result in the emerging technology becoming legally and/or economically unviable.[29]

One way to account for technological changes would be to construct the regulatory instruments in a technology-neutral manner, resulting in a system of governance that does not discriminate between different technologies, nor does it become obsolete when faced with technological advancement. The global patent system has adopted this approach of technology neutrality[30], as exemplified by Article 52(1) of the European Patent Convention (EPC) and Article 27(1) of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement). This approach is not without its critics. Bennett Moses argues that neutral drafting techniques are inherently limited, especially in situations in which they merely ensure non-discrimination at the cost of efficiency.[31] In a similar vein, Claudia Schmidt concludes that ensuring efficiency in IPR systems requires some level of differentiation between technologies.[32] Burk and Lemley go even further by stating that this is the *de facto* reality of patent law, as in practice, patent systems are anything but technology neutral.[33] In order to provide an answer to this dichotomy, it is necessary to analyze whether the current European patent system offers efficient solutions to the issues raised by synthetic biology. This very pursuit constitutes the first step of inquiry in this thesis.

If we assume that synthetic biology does indeed exhibit a potential pacing problem that technology-neutral drafting techniques are unable to manage, the second logical step in such

[28] Marchant 2011, p. 23.
[29] *Idem.*, p. 25.
[30] van den Belt 2014, p. 25–26.
[31] Bennett Moses 2007, p. 274.
[32] Schmidt, C 2011, p. 55.
[33] Burk & Lemley 2003, p. 9.

an inquiry is to determine a course of action that would ameliorate any such incompatibilities. This necessitates an understanding of the incentive structures of the innovators themselves. Assuming that Marchant is correct about the risks posed by the pacing problem, should one attempt to resolve the problem *ex post* on a case by case basis, or should one endeavor to construct some coherent *ex ante* framework to guide the work of legislators, regulators, and adjudicators?

Scholarly opinion would strongly seem to favor the latter. Minssen et al. have noted that due to the increasing complexity of the legal issues generated by synthetic biology IPRs, an *ex ante* approach to deal with foreseeable problems is mandated.[34] Mandel has warned against dealing with such issues *ex post*, instead advocating "an iterative process at early stages of technological development and commercialization"[35]. This system consists of adopting an initial framework of governance, followed by data collection, evaluation and modification of the framework.[36] As synthetic biology is still in its nascence as a technology[37], it possible to affect its developmental course in this way. Following Mandel's recommendation, the second step of this inquiry is to determine what such an *ex ante* framework of synthetic biology IPR governance should be.

One question remains: how far should one go in creating such a framework? In their commentary, Ludlow et al. have opined that when faced with a pacing problem, wholesale changes to systems of governance are unlikely to succeed.[38] Following this caveat creates an additional criterion for any proposed framework of synthetic biology IPR governance: simplicity. A proactive approach that can be enacted through minor legislative, regulatory, institutional or judicial changes, or even entirely non-institutional means, is preferred. Such methods are also more amenable to the subsequent modifications required in Mandel's model. A vital boundary condition is to ensure that the basic structure of the patent system, such as technology neutrality, is not extended beyond what is absolutely necessary.

1.3. Research questions

The discussion in the preceding section serves as a conceptual outline for the research questions of this thesis. As a reminder, the first step of inquiry is to determine whether

[34] Minssen *et al.* 2015, p. 237.
[35] Mandel 2009, p. 89.
[36] *Idem.*, p. 89.
[37] Mandel & Marchant 2014, p. 156.
[38] Ludlow *et al.* 2015, p. 161.

synthetic biology as a technology is somehow ill-suited for the existing forms of IP governance and management in Europe. This general question can be subdivided into a set of more specific research questions. The following listing is for illustrative purposes only, not intended to be taken as arising *ex nihilo*. The provenance of these interconnected issues will become evident in the following chapters of this work.

Is synthetic biology a special case? The first step of inquiry must build upon a solid understanding of the technology itself, what its current developmental state is, what types of actors exist within the synthetic biology research community, and what types of IPR management practices that community has adopted.

How does synthetic biology relate to European patent law? A fundamental starting point in any prescriptive inquiry is to establish what the current state of affairs is. Given the topic at hand, the most important question is how synthetic biology inventions fit into the current European patent system. This requires a basic understanding of the relevant European legislation and agreements, what specific issues arise in the interpretation of those sources of law, and what the actual state the technology is in terms of patents granted.

What is the purpose of patent protection? To determine whether the European patent system operates acceptably well in relation to synthetic biology, it is necessary to have some standard of measurement. Developing such a standard requires an understanding of the underlying purpose of patent protection. If modifications to the patent system are warranted, they will be compared to the existing system in relation to the same standard.

Patent fragmentation and overlap. As with other forms of biotechnology, synthetic biology is subject to high levels of patenting.[39] A single gene may be subject to several patents[40], and the research tools required to study and modify it might be proprietary as well[41]. Given that any one of the patent holders can potentially block the development of new innovations that are based on prior ones, does this result in the current patent system generating suboptimal outcomes? If so, does this affect the development of synthetic biology innovations? Answering these questions requires an analysis on the potential of synthetic biology to exhibit such problems. If it does, it is necessary to determine the factors that contribute to it.

[39] Kumar & Rai 2007, p. 1751–1762.
[40] Merz & Cho 2005, p. 205.
[41] Wang 2008, p. 253.

Transaction costs. Assuming that synthetic biology does suffer from a fragmented patent landscape, how does this affect the various transaction costs involved in the research and development (R&D) and commercialization of innovations within the field? This requires determining what types of transaction costs are relevant and what their likely effects are.

Collective action. Assuming that synthetic biology exhibits fragmentation and high levels of detrimental transaction costs, it is necessary to determine whether those issues can be sufficiently resolved by market forces operating in line with the current patent system. This requires an understanding of the incentive structures of the market actors involved in synthetic biology development.

Provided that synthetic biology exhibits the aforementioned problems, the second stage of inquiry is to construct a framework of governance that addresses those issues in an efficient manner. The analysis conducted in the previous stage of inquiry provides the necessary backdrop for this process. Because of the limitations arising from the necessity of a relatively simple solution, it is not possible to construct a novel *sui generis* form of IPR protection that would replace the patent system in its entirety. Instead, a variety of existing solutions or novel solutions that are broadly in line with current patent legislation are be analyzed and addressed, with the objective of finding a combination that best ensures the functionality of both synthetic biology and the patent system. The final product of this part of the inquiry consists of concrete policy and legislative suggestions.

1.4. Demarcation

Providing an exhaustive answer to the full spectrum of all possible SynBio IPR concerns requires an analysis far too broad to fit within this work. Instead, the primary emphasis will be on *the efficiency of European patenting system and patent practices in synthetic biology.* The *European* dimension means that legislation and court decisions from other countries and institutions are utilized for comparative purposes, but the definite emphasis is on Europe as a whole. This results in the highlighting of the European Patent Convention as well as EU legislation, with some minor references to national law.

As synthetic biology has the potential to create new lifeforms or redesign existing ones, it has generated a great deal of interest in both bioethics[42] and biosecurity.[43] After all, the editing and patenting of organisms and their constituent genetic material is one of the major

[42] See *e.g.*: Boldt 2016, *passim* for an overview of the bioethical debate.
[43] See *e.g.*: Winter 2015 *passim* for an overview of the biosafety debate.

topics in current bioethics.[44] As for biosafety, synthetic biology shares a definite legislative boundary with existing European GMO regulations.[45] While both these issues do have dimensions in IP law, they are not central to it, especially given that the emphasis of this work is on *efficiency*. Consequently, neither topic will be discussed in this work. The nature of the technology, as well as the aforementioned economic emphasis results in questions relating to fundamental rights being omitted. While highly important, they require an entirely different approach.

Emphasizing *patent law* will exclude any broad discussions on issues such as DNA copyright. The emphasis on patent law is justified by the fact that, despite attempts, copyright authorities have yet to allow the extension of copyright to DNA sequences.[46] A second justification lies in the fact that creators of SynBio applications seeking proprietary forms of IPR protection have done so by applying for patents.[47] This thesis will include some minor references to DNA copyright, but only for the purposes of illustrating some of the conceptual difficulties inherent in synthetic biology.

Even though it is conceivable that synthetic biology inventions could include synthetic alterations to the genomes of humans and animals[48], the emphasis on *synthetic biology* means that similar issues raised in other fields of European biotechnology patenting scholarship are consciously omitted from discussion. Addressing them would require an extensive discussion on issues that are highly complex in their own right, such as germ-line modifications, cloning, and the patentability of embryos.[49] These issues are not specific to the efficiency of the European patent system in relation to synthetic biology.

1.5. Field of law, methodology, and sources

Given the aims of this thesis, the general field of law most relevant to it is intellectual property law, with a special emphasis on *European patent law*. Patent law is primarily concerned with the questions of what can be patented, how a patent is granted, and what the ensuing legal effects of patents are. The period of exclusivity following the granting of a

[44] See *e.g.*: Stazi 2015, p. 49–56; Brody 2007, *passim.*
[45] Douglas & Stemerding 2014, p. 7–9.
[46] See *e.g.*: Holman *et al.* 2016, *passim.* N.B.: This issue has not been similarly raised in Europe, presumably due to the fact that full copyright protection in Europe is automated.
[47] See *e.g.*: Nature SynBio Patent Grants 2015, p. 822.
[48] See *e.g.*: Frow & Calvert 2013, p. 37, in which professionals within the field discussed the potential of synthetic biology to develop lava lamps made of color-changing mice, television-tortoise hybrids, and miniature fighting dinosaurs.
[49] See *e.g.*: Stazi 2015, *passim* for a thorough introduction to these topics.

patent might considerably improve the market power of the patentee[50], which naturally results in a reduction of competition in the relevant market. Because of the interrelatedness of innovation, market power, and competition, any attempt to address these issues cannot hope to succeed without some elements of *competition law*.[51] Both the European scope of the patents discussed as well as the harmonized nature of competition law mandates the inclusion of general *EU law*.

The methodologies of legal research adopted in this thesis seek to provide a means of addressing the constituent parts of its objective, namely efficiency and European patent law. In this respect, the two steps of inquiry raise an important epistemological point: the first point of inquiry is inherently descriptive, whereas the second one requires a formulation of normative statements. In such contexts, one is well to be reminded of Hume's guillotine, which states that normative statements do not follow directly from descriptive statements, or more simply put: *"there is no 'ought' from 'is'"*[52]. Ensuring the validity of the arguments contained herein requires a methodological approach in which the descriptive nature of patents in synthetic biology is demarcated from the normative proposals. The descriptive section of this thesis is built upon common approaches in Nordic jurisprudence, namely legal dogmatics, comparative law and the economic analysis of law. The normative statements formulated in the latter part of this thesis rely primarily on law and economics.

The reason for including an economical perspective is that the analytic study of optimal efficiency is a long-established sector of welfare economics[53], making it the most suitable candidate for any such endeavor. It also provides this inquiry with the requisite tools to answer a large portion of the specific research questions outlined in chapter 1.3., such as the purpose of the patent system and the nature of the intellectual property problems engendered within synthetic biology. Building on a set of underlying assumptions, the economic analysis of law also allows the formulation of prescriptive policy solutions without falling victim to Hume's guillotine. The validity of any such suggestions is contingent on the legitimacy of the underlying assumptions employed by the economic model.[54] As the aim is to improve welfare through ensuring the viability of synthetic biology, the variety of economics used is *welfare economics*, an approach that seeks the maximization of aggregate welfare through

[50] Landes & Posner 1981, p. 943.
[51] See *e.g.*: Anderman 2011 p. 105–128 on the interface of EU competition law and IP law.
[52] Tontti 1998, p. 35–36.
[53] Motta 2004, p. 18.
[54] See: Appendix 1 for the discussion on the assumptions used in this thesis.

ensuring optimal efficiency.[55] This is the fundamental starting point for creating a standard of efficiency for the patent system, both in evaluating its potential problems and in creating proposals for patent policy and *de lege ferenda* that improve upon them. The assumptions entailed by welfare economics also result in several criteria of falsification for both the descriptive and normative analysis, adding an element of the Popperian scientific method[56] which often is omitted from legal analyses.

Legal dogmatics concerns itself with the systematization and interpretation of existing legal norms.[57] The tradition of legal dogmatics that will be evidenced in this work is an applied version of Aarino's neorealistic approach.[58] It will be the method of choice for identifying and interpreting the existing norms of European patent law. However, the use of legal dogmatics will be limited to pure description, as it does not allow for the creation of the types of normative proposals that this thesis is aiming for, which are fundamentally based on the economics of innovation.

A minor comparative approach is also called for. Most of the research in synthetic biology has taken place in the United States of America.[59] Consequently, a large segment of the academic literature pertaining to the legal and economic aspects of synthetic biology are of American origin. This approach is also justified by the fact that certain aspects of European and US patent law have been harmonized through the 1995 Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). However, there are some important differences between the European and US systems which limit the use of comparison as a normative tool. The systems have different ways of managing the tension between the pro-innovative but anti-competitive aspects of patents. The United States favors an IPR-friendly approach, whereas the European system is more geared towards ensuring competition.[60]

The sources for this thesis consist primarily of journal articles in both patent law and law & economics journals, as well as monographs on such issues. Due to the difference in the pace of development within the field, the primary sources on SynBio patent economics are mostly of American origin, whereas the newer literature is primarily European. In regards to the biotechnological source literature, a concentrated effort has been made to utilize sources of

[55] See *e.g.*: Hicks 1939, p. 698–712 for an overview of the foundations of welfare economics.
[56] See *e.g.*: Blaug 1994, p. 109 regarding the importance of falsifiability criteria in economics.
[57] Hirvonen 2011, p. 25–26.
[58] Aarnio 1997, p. 49–52.
[59] Oldham et al. 2012, p. 6.
[60] Tudor 2012, p. 225

the highest possible quality, such as recent publications in the journals *Nature* and *Science*. Other such citations are based on highly-esteemed and widely used reference manuals, which supplement these articles by providing necessary background information regarding the basics of molecular biosciences.

1.6. Background concepts

1.6.1. Upstream and downstream patents

Modern biotechnological innovation can be conceptually divided into three stages: basic research or initial innovation, follow-on research, and commercialization.[61]. It is often so that each of the three stages requires both inventions from the preceding stage and older innovations from the same stage as inputs.[62] Especially in rapidly developing fields, such as biotechnology, such preceding inventions may still fall under patent protection. This results in a hierarchy of patents, in which innovators must obtain licenses for patented inventions in order to develop their own invention. This allows for a way to describe the contents of this hierarchy as *upstream patents* and *downstream patents*.

Holman offers a generalized definition of upstream patents as "patents that claim technologies associated with basic and early stage research and development, as opposed to patents covering 'downstream' commercial products"[63]. Resnik describes upstream patents as those vital for the development of a multitude of other inventions, which in turn may be upstream inventions for future applications.[64] Resnik cites the example of a transistor being an upstream invention of a microchip, which in turn might be an upstream invention in a downstream commercial product, such as a mobile phone.[65]

1.6.2. Complementary, substitute, blocking and essential patents

Complements and substitutes are general economic concepts that have been extended to cover aspects of patent law. Complementary goods are goods that have little to no use or value unless coupled with some other commodity[66], such as cars and tires. Substitute goods are goods which can be used as replacements for each other[67], such as butter and margarine.

[61] Wang 2008, p. 266.
[62] *Idem.* p. 261.
[63] Holman 2006, p. 629.
[64] Resnik 2003, in footnote 22.
[65] *Idem.*
[66] Cooter & Ulen 2004, p. 182
[67] Posner 2003, p. 43.

In patent law, complementary is evident when a new invention requires the integration of two or more inventions as its inputs, with each of those specific inventions being indispensable in the development of the downstream invention. Patents for such upstream inventions are appropriately called *complementary patents.*[68] Substitution is possible when two or more inventions may be used as replacements for each other, with only one of the many substitute technologies being necessary for the development of the downstream invention. Concordantly, patents for such technologies are called *substitute patents.*[69]

When attempting to acquire licenses for complementary patents, it may be the case that one of the patentees refuses to license their invention. If the upstream patents are truly complementary, this means that the development of any new technology reliant on such patents will be blocked. Such patents are called *blocking patents*.[70] One additional caveat is necessary. The relevant literature generally considers the terms 'essential patent' and 'blocking patent' to be synonyms.[71] European legislative text operates under a similar definition, but distinguishes between patents for a) technologies that are essential for the creation of a product and b) those that are essential for conforming to a technological standard.[72] For reasons of clarity, this thesis will follow the European legislative distinction, with *essential patent* denoting the former and *standard-essential patent* denoting the latter.

1.6.3. Regarding economic concepts

As stated in the methodology section, this thesis relies heavily on economic analysis. Such an approach inherently requires a substantial discussion on the underlying assumptions and concepts that come with any attempt at the economic analysis of law. For the purposes of this thesis, the most important of these are *rational choice theory* and *efficiency.* However, a full definition and justification of these concepts would result in a digressionary segment of considerable length. Including such a segment into this introduction would distract the reader from the fundamental aims of this work, resulting in poor legibility. That does not mean that a proper analysis on such important economic concepts is omitted. The discussion relating to the aforementioned concepts can be found in Appendix 1 of this thesis.

[68] Schmidt, K. 2014, p. 68.
[69] WIPO Patent Pools Analysis, p. 4, Section II.a.8.
[70] Shapiro 2001, p. 120.
[71] See *e.g.*: Motta 2004, p. 206; Shapiro 2001, p. 134.
[72] See *e.g.*: TTA Guidelines, para. 252.

1.7. Structure of proceedings

The general assumption in this thesis is that the reader is moderately well versed in the basic structure of patent law; its primary focus is on the law and economics of patents. Chapters and sections detailing the norm structure of the European patent system are consequently brief, with the focus being on how the norms relate to synthetic biology. The structure broadly follows the order of the research questions. However, the interconnectedness of those questions means that they cannot be discussed entirely separately. This thesis seeks to adopt a more logical way of discussing the issues, allowing the reader to follow the text without undue complications, but which results in the answering of the research questions.

The second and third chapters are the main descriptive chapters of this thesis. The second chapter offers an introduction to the technology of synthetic biology. This chapter seeks to answer the question of why synthetic biology is a special case. After reading that chapter, it is hoped that the reader understands the general nature of the technology, what its potential and limitations are, how it relates to existing forms of intellectual property protection, as well as how the practitioners within the field view IPR protection. The third chapter seeks to set synthetic biology firmly in the existing framework of European patent law, with a special emphasis on the EPC. This chapter seeks to address the issue of the patentability of synthetic biology. In addition, this chapter seeks to outline some issues that synthetic biology might face when interpreted through EU and EPO case law.

The fourth chapter consist of patent economics. The first part of this chapter aims to provide both a descriptive economic analysis of biotechnological patenting in general and synthetic biology in particular. The objective is to introduce the reader to the economic rationale of patents, as well as to explain why synthetic biology patenting may result in fragmentation and overlap, as well as increased transaction costs. The fifth chapter continues this analysis, seeking a general outline for normative solutions to these problems, seeking to construct the normative criterion used to evaluate the efficacy of the patent system. The sixth chapter centers on a discussion on the tools that the free market, patent policymakers, and legislators have at their disposal to enact the normative logic of the previous chapter. The first part of the sixth chapter examines the efficacy of the free-market tools and their optimally construction. The latter part of the chapter is centered on what changes to existing policy and law are required for solving the problems outlined in the previous chapters.

2. Synthetic biology as a technology

2.1. A conceptual understanding

Synthetic biology (SynBio) seeks to combine the innovations of biotechnology with approaches adopted from fields such as electrical and semiconductor engineering[73], computer and software engineering[74], and nanotechnology.[75] The fundamental aim of this technology is to standardize biological systems into discrete units with clearly defined and predictable qualities, thus allowing the creation of functional designer devices and novel biological systems from a set of standardized and modular constituent parts.[76] Because of the cross-disciplinary nature of synthetic biology, it is difficult to define in exact terms. While undoubtedly an extension of current practices in biotechnology, many commenters have highlighted the difficulty of differentiating between synthetic biology and other related disciplines, such as genetic and metabolic engineering.[77] Some general idea of what makes synthetic biology unique can gained through comparing it to its technological predecessors.

The connection to biotechnology, especially recombinant DNA technology, arises from the fact that synthetic biologists utilize DNA and other biological substances as their primary source materials[78], which are then modified and edited to suit their needs. However, the addition of engineering principles differentiates it from previous forms of biotechnology. The key difference between the aforementioned rDNA technologies and synthetic biology is that the former results in genetically altered variants of existing organisms, whereas synthetic biology allows for the rational creation and design of entirely new organisms with properties that do not currently exist in nature.[79] The engineering principles of modularity and standardization invite analogies to semiconductor and computer technologies, in which a more complicated system is constructed of standardized parts.[80] The link with software lies in the fact that assembling such modular parts into devices and systems is an inherently creative endeavor, with various ways of assembling standardized constituent parts that results in a system that performs a specific task.[81] Synthetic biology relates to

[73] Dutfield 2012, p. 125.
[74] Torrance 2010, p. 635–636.
[75] Torgersen & Schmidt 2013, p. 47.
[76] Weber & Fussenegger 2012, p. 21.
[77] See *e.g.*: Fernandez y Brañas 2014, p. 188–189.
[78] Mandel & Marchant 2014, p.159.
[79] Schmidt, J. 2016, p. 15.
[80] Dutfield 2012, p. 125.
[81] Agovic 2014, p. 103.

nanotechnology through similar objectives in constructing molecular mechanical devices that operate independently. The difference between the approaches is that in synthetic biology, the devices constructed are of a fundamentally biological nature.[82]

Many of the aforementioned precursors of synthetic biology, such as the semiconductor industry, are regarded as being a *complex technologies.*[83] The nature of this complexity lies in the fact in such technologies, downstream inventions contain multiple separately patentable (or indeed, patented) elements.[84] The complexity of a given technology also indicates that technological development in the field is dependent on upstream innovations, with each subsequent invention resulting from what is inherently a cumulative process of research and development.[85] This can be contrasted with more traditional *discrete technologies*, in which an invention combines relatively few patentable elements.[86] A commonly used example of the latter is a pharmaceutical compound.[87] The shared underlying idea of having multiple patented technologies as inputs for subsequent innovation results in the inextricable interrelatedness of the previously mentioned concepts of complex technologies, cumulative innovation, complementarity, and upstream patenting. As a combination of multiple complex technologies, synthetic biology could even be described as a 'hypercomplex' or 'metacomplex' technology.

2.1.1. Definitions for synthetic biology

The previous outline provides some notion of what makes synthetic biology unique. However, a generalized concept is insufficient for creating a functional system of intellectual property governance for such a technology, as it would be impossible to determine which issues function acceptably well within existing IP systems and which issues require genuinely novel solutions. Despite a great deal of academic debate, no wide consensus exists on such a definition.[88] In such a situation, it would normally be sensible to adopt the definition constructed by an institutional entity that has the power to effect legislative and regulatory change. Such definitions do exist. A pertinent example would be the following definition adopted by the European Union:

[82] Koepsell 2014, p. 46–49.
[83] von Graevenitz *et al.* 2011, p. 9.
[84] Cohen et al. 2000, p. 9.
[85] *Idem.* p. 19.
[86] *Idem.*, p. 9.
[87] von Graevenitz *et al.* 2011, p. 9.
[88] Oldham et al. 2012, p. 3.

> *"Synthetic biology is the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms."*[89]

This definition, while brief, is too general to effectively distinguish synthetic biology from other forms of biotechnology. The co-founder of synthetic biology, Timothy S. Gardner, has criticized this trend towards overly broad definitions which increase the risk of conflating synthetic biology with more traditional biotechnology, therefore robbing the former of its unique characteristics. This may hamper any regulatory efforts targeted specifically towards the creation of a constructive framework for synthetic biology.[90] Gardner calls for a return to the foundational idea of SynBio, namely "the standardization and abstraction of biological components"[91]. Another way to resolve the issue is to view synthetic biology as a collection of broadly similar approaches. One such definition is offered by Markus Schmidt, who divides SynBio into the subfields of: 1) DNA synthesis, 2) design of DNA-based biological circuits, 3) minimal genome design, 4) protocell development, and 5) xenobiology.[92]

The focus of this thesis will be on the so-called *bioparts approach*, which combines elements 2 and 3 of Schmidt's definition with the underlying rationale of Gardner's general definition. With this in mind, it is necessary to give an operational definition of synthetic biology for the purposes of this thesis. The definition given below is a combination of the applicable parts of the three definitions discussed above:

> Synthetic biology is the science of the standardization and abstraction of biological material through the utilization of engineering principles. Such biological material may be synthetically constructed or derived from naturally occurring sources. One of the subfields of this general endeavor is the formation of a hierarchy of interchangeable, modular and discrete bioparts, devices and systems (*bioparts approach*). These elements are implemented in a chassis, which subsequently performs a biological function.

[89] Opinion on Synthetic Biology I, p. 30.
[90] Gardner & Hawkins 2013, p. 871.
[91] *Idem.* p. 872.
[92] Schmidt M. 2011, p. 112–113.

2.1.2. Bioparts approach

A full understanding of the definition given above requires a description of the bioparts approach. *(Bio)parts*[93] are the semi-literal building blocks of this form of synthetic biology. The term is generally understood to mean a strand of synthetically designed DNA that encodes a biological function[94], such as a synthetic gene that produces a synthetic protein. Such a DNA sequence may conceivably be either constructed *de novo* or be a modified variant of an existing DNA sequence created through recombinant DNA technology.[95] A common analogy used to clarify the nature of bioparts is to compare them to biological Lego bricks.[96] *Devices* are combinations of bioparts, which together perform some specific biological function that is of human definition and design.[97] An example of a device is a combination of bioparts that can perform Boolean algebra, such as a biological XOR logic gate.[98] *Systems* are combinations of devices and parts that perform actual tasks[99], such as computation. As an example, through a combination of AND, XOR and OR biological logic gates[100] (i.e. devices as defined above), it is possible to construct a biological system that has the same basic computational structure as a conventional computer.[101]

In order to perform their functions and tasks, the aforementioned elements must be implemented in some biological system, most commonly a modified microbe such as *Escherichia coli*.[102] The microbe in which the biosystems are implemented is called the *chassis*.[103] The modifications to the chassis commonly consist of removing all extraneous genetic material that the microbe does not require to sustain itself, thus creating a *minimal genome*[104], as well as making modifications to existing metabolic pathways[105].

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[93] *N.B*. The literature is not consistent in its terminology, with variable use of the terms 'part', 'biopart' and 'biobrick' (if in lower case) all denoting the same basic concept. For purposes of clarity, this thesis will refer to these components as 'bioparts', following the nomenclature of *i.a*. Winter 2016, p. 172.
[94] Baldwin *et al.* 2016, p. 20.
[95] *N.B*. Complementary DNA strands based on unmodified DNA/RNA, while not existing in nature, are generally not considered to be examples of synthetic biology, as they lack modular design.
[96] See *e.g.*: Winter 2016, p. 172.
[97] Baldwin et al. 2016, p. 20.
[98] See: Rubens et al. 2016, p. 5 for an example of a SynBio XOR gate device.
[99] Baldwin *et al.* 2016, p. 20.
[100] *N.B.:* Specifically a so-called *binary full-adder*.
[101] See: University of Seoul Project Page on how Korean students designed precisely such a system in the 2012 iGEM competition.
[102] See *e.g.*: Khalil & Collins 2010 *passim.*
[103] Baldwin *et al.* 2015, p. 162.
[104] Selgelid & Evans 2015, p. 3.
[105] Opinion on Synthetic Biology II, p. 29–31.

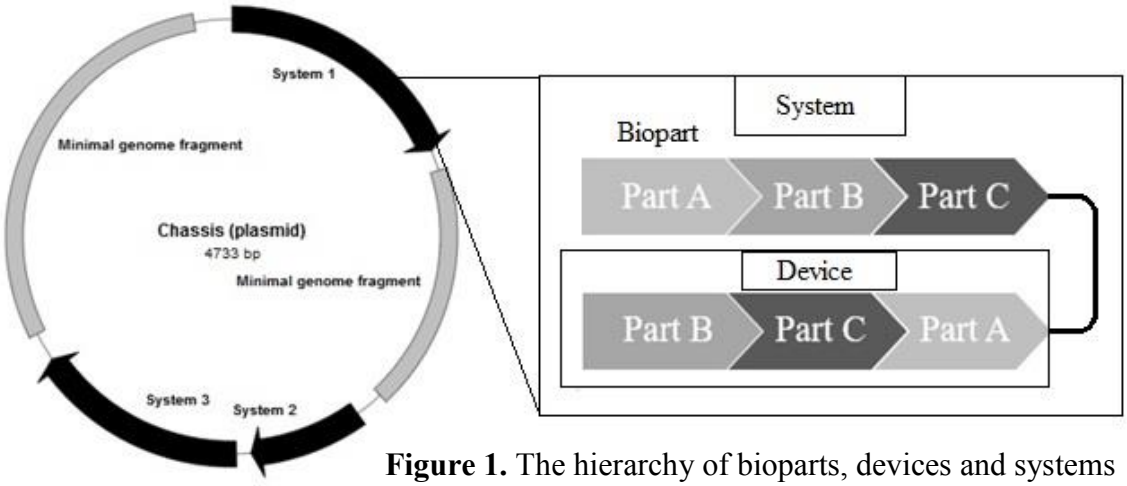

Figure 1. The hierarchy of bioparts, devices and systems as implemented in a chassis.

2.2. Legal frames for synthetic biology IPs

Being an outgrowth of several different technological traditions, synthetic biology is also unique in how it has the potential to combine different intellectual property rights.[106] This leads to the following question: should synthetic biology primarily be viewed as an extension of biotechnology and other similar engineering fields into more creative ones, such as software engineering, or vice versa? Choosing either frame results in very different implications for IPR protection. Viewing synthetic biology as an extension of established biotechnology, such as rDNA technology, sets it squarely in the field of patent law. Another possibility would be to frame the issue in relation to either open source or proprietary software, in which the most relevant IP structure is copyright. Neither of these frames can be dismissed out of hand, it is necessary to analyze each of them separately.

Possibly the simplest solution is to adopt a historical perspective, in which synthetic biology is viewed primarily as a form of "extreme genetic engineering"[107]. As a subfield of biotechnology, it shares many of features with its parent technology, such as various genetic engineering techniques.[108] This choice of frame results in viewing synthetic biology solely through the lens of the existing system of biotechnological patent protection, as that is the IP instrument most relevant to its predecessor field.[109] As stated in the introduction, this is the approach chosen in this thesis, which is justified by the aforementioned fact that patents are the *de facto* form of proprietary IP protection within SynBio.

[106] Torrance & Kahl 2014, 221–228.
[107] ETC Group, Report on Synthetic Biology 2007, p. 4.
[108] Robienski & Simon 2014, p. 127–128.
[109] Baldwin *et al.* 2015, p. 137.

It is worth noting that many applications of synthetic biology manage to sidestep some of the most contentious intellectual property issues in modern biotechnology.[110] As synthetic biologists concern themselves with more or less synthetic constructs, they are not similarly subject to the worldwide debate regarding the patentability of isolated human DNA sequences and whether they should be considered inventions or discoveries.[111] This is not to say that SynBio is free of all the problems plaguing traditional biotechnology. A great deal of legal-economic scholarship has been devoted to economically detrimental patenting practices in biotechnology, which may affect synthetic biology as well, possibly in an exacerbated form. An example of such a problem is overly broad patent applications, such as the European patent application by the J. Craig Venter Institute for synthetic biology tools relating to the creation of micro-organisms with minimal genomes.[112]

If synthetic DNA is viewed as a coding medium for biological programs, it makes sense to compare it to software. This in turn raises the issue of copyright, which in most cases is the IPR *de rigueur* in that field.[113] A common argument that advocates this frame is that writing and designing synthetic DNA sequences has an element of choice, which can only be described as artistic expression.[114] In second, synthetic DNA may be used as a storage medium for materials which are undoubtedly copyrightable, such as creative works. As an example of the latter, research groups have encoded *inter alia* books[115] audio files[116], and even a computer operating system[117] into DNA. These strands of synthetic DNA could conceivably be amplified using the polymerase chain reaction (PCR) method, resulting in millions of strands of DNA[118], which could subsequently be decoded into binary form and represented as audio, text or fully functional software. In such situations, it is easy to note the potential for a full-on collision of patentability and copyright.

Despite the *de lege lata* solution that highlights the primacy of patents over copyright in biotechnology, the conceptual conflict of the examples given above is not without

[110] OECD SynBio Report 2014, p. 96.
[111] See e.g.: Stazi 2015, p. 145–165 and 220–224 for overview of the legal debate in the US and Europe.
[112] EPO patent application EP 06825527, extension of WIPO patent WO2007047148. *N.B.*: the EPO Examining Division responsible for the application deemed it insufficient in terms of novelty, inventive step, and disclosure. The application was deemed withdrawn as of May 2012. See also: Fernandez y Brañas 2014, p. 191.
[113] See *e.g.*: Article 4 of the WIPO Copyright Treaty of 20 December 1996.
[114] Rai & Boyle 2007, p. 389–392.
[115] Church *et al.* 2012, p. 1628.
[116] Goldman et al. 2013, p. 77.
[117] Erlich & Zielinski 2017, p. 951.
[118] See e.g.: Glick *et al.* 2010, p. 108–117 for a description of how the PCR method functions.

importance. Multitudes of scholars have raised concerns that synthetic biology may be systemically incompatible with the current paradigm of IPR protection.[119] Commentators such as Palombi have highlighted the possible need of creating a *sui generis* form of IPR protection for genetic sequences in general[120], which would necessarily extend to synthetic biology as well. However, as stated in chapter 1.4., this thesis will not feature any extensive discussion on DNA copyright, nor will it adopt a constructivist approach for entirely novel *sui generis* models.

2.3. The potential of synthetic biology

Proponents of synthetic biology often highlight the transformational potential of the technology. Advocates such as Khalil and Collins have stated that while synthetic biology faces some daunting technological challenges, their resolution would lead to a situation in which the technology is limited "only by the imagination of researches and the number of societal problems and the applications that synthetic biology can resolve"[121]. This potential has led to intensive research efforts in various fields, three of which will be mentioned in this context. Arguably the most prominent and promising application of synthetic biology is in solving many issues that relate to human health.[122] A second potential and highly researched application of synthetic biology is in developing renewable sources of bioenergy through the production of biofuels by synthetic microbes.[123] A third field of study involves the creation of cellular computers.[124] For the sake of brevity, only the first of these will be discussed in more detail.

Researchers and scholars have outlined several different modalities in which synthetic biology may have a positive impact on human health. To this effect, van Passel et al. outline the following instances of synthetic biology that have some existing applications: the microbial production of drugs, fighting infections, the treatment of genetic disorders, sensing environmental pollutants, infection detection, cancer treatments, and the development of biohybrid materials that enhance drug administration.[125] While undoubtedly interesting, a lengthy exposition on each of these applications falls well beyond the purpose of this thesis.

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[119] See *e.g.*: Minssen et al. 2015 *passim*; Thambisetty 2013 *passim*; Kumar & Rai 2007, p. 1748–1762.
[120] Palombi 2008, *passim.*
[121] Khalil & Collins 2010, p. 377.
[122] See *e.g.*: Henkel & Lüttke 2014, *passim.*
[123] See *e.g.*: Mandel & Marchant 2014, p. 165–169.
[124] See *e.g.*: Service 2013 *passim.*
[125] van Passel et al. 2014, p. 4–8. For a more thorough listing of the biomedical applications of synthetic biology, see: Weber & Fussenegger 2012 *passim*.

In this instance, an example of the microbial production of drugs is sufficient to give the reader some concept of the scientific and technical developments in the field.

An oft-quoted breakthrough in this application of synthetic biology was the production of semi-synthetic *artemisinin*. Artemisinin forms the basis of the WHO-recommended treatment of malaria caused by the parasite *P. falciparum*, specifically in the form of artemisinin-based combination therapies (ACTs)[126]. Artemisinin was previously sourced exclusively through extracting it from the plant *Artemisia annua*, an important cash crop in many developing countries.[127] Despite the drug having been produced on a non-profit basis by the pharmaceutical companies Novartis and Sanofi-Aventis, the cost of the drug (4-10$) was considered prohibitively high for patients in high-risk areas.[128] In 2006, researchers from Amyris Biotechnologies combined a total of ten different genes sourced from bacteria, plants and yeasts into a modified *S. cerevisiae*-based chassis organism, more commonly known as Brewer's yeast. This modified yeast produced high concentrations of a precursor of artemisinin through a semi-synthetic mevalonate pathway that converted acetyl coenzyme A into artemisinic acid[129], which in turn could be chemically synthesized into artemisinin.[130]

The reason why this was considered a triumph of synthetic biology instead of rDNA technology was primarily due to the scale of the genetic engineering. Ro et al. introduced a total of 10 genes[131], compared to the single modifications more common in traditional applications of rDNA technology. In addition to the scale of the genetic material transferred, the researches made modifications to the metabolic pathways of the semisynthetic yeast that resulted in maximizing the yield of arteminisic acid and minimizing the production of cytotoxic compounds, such as artemisinic aldehyde.[132] When utilizing the modified yeast, artemisinin production required roughly the same biomass as when sourced from *A. annua*, but with a significantly higher rate of production; 4-5 days instead of 8 months.[133]

This example above should be taken with a grain of salt. It can be argued that it is not a true manifestation of synthetic biology, as it did not exhibit much in the way of standardization

[126] WHO Malaria Guidelines 2015, *passim.*
[127] van den Belt 2014, p. 20.
[128] van Passel et al. 2013, p. 4.
[129] *N.B.:* the fact that the modified S. cerevisiae produced a precursor of artemisinin is what made the process semi-synthetic. A true biosynthetic process would have resulted in the production of artemisinin. See: Paddon & Keasling 2014, p. 364.
[130] Ro *et al.* 2006, p. 940–941.
[131] *Idem.*
[132] Paddon & Keasling 2014. p. 362.
[133] van Passel *et al.* 2014, p. 4.

or modularity in the genes transferred nor the chassis used.[134] This skepticism should be extended to cover the field in general. Multiple commentators have noted that however high the promise of synthetic biology may be, it relies on the idea that biological material can be standardized. It might turn out that biology is inherently too chaotic and unpredictable to be categorized and modelled in a sensible way.[135] Whether one chooses to take a skeptical or optimistic view of the prospects of synthetic biology, it is hard to deny that those prospects should be explored. It does require that we acknowledge that its high potential exists in combination with the unknown limits of how much engineering nature can accommodate. This translates to a high level of economic risk for anyone engaging in such research, which in turn requires economic incentives. In biotechnology, such incentives are often generated by the aforementioned intellectual property rights, especially patents.[136]

2.4. SynBio inventions as property and commons

The synthetic biology community is divided in its attitudes towards IPR protection. Unlike many fields of biotechnology, which have traditionally favored strong patent protection[137], a large part of the research community involved in synthetic biology maintains a strong commitment to keeping the field as unhindered by IPRs as possible.[138] This type of commons approach (commonly referred to as *access to knowledge* or *A2K*) is characterized by researchers such as Drew Endy and Tom Knight, who have sought to construct a communal system that allows for the free sharing of information between research initiatives, especially regarding upstream research.[139] The commons model is embodied by the three inter-related institutions of the BioBricks Foundation, The Registry of Standard Biological Parts, and the iGEM competition.[140] The commons approach is contrasted by institutions such as the aforementioned J. Craig Venter Institute, which have sought strong patent protections for their SynBio inventions, such as the synthetic chassis *mycoplasma laboratorium* described in the very first words of this thesis.[141] This approach is henceforth referred to as the *IP frame*.[142] What follows is a brief overview of these two models.

[134] Kelle 2013, p. 1126.
[135] Kahn 2011, *passim.*
[136] Stazi 2015, p. 6.
[137] Baldwin *et al.* 2015, p. 137.
[138] Torrance 2010, p. 653.
[139] Calvert 2012, p. 175–176.
[140] Torrance 2010, p. 656–657.
[141] Van den Belt 2013, p. 90–93.
[142] See: van den Belt 2013, p. 90 for the nomenclature of IP vs. A2K in relation to SynBio used herein.

2.4.1. IP frame vs. A2K

The IP frame in synthetic biology is in essence an extension of the current paradigm of the biotechnology industry in seeking strong proprietary IPRs for their inventions, which is especially visible in the patenting of genes.[143]As can be inferred from the previous paragraph, arguably the most famous proponent of the proprietary model of SynBio innovation is J. Craig Venter and the institutes and companies he is associated with, *inter alia* the J. Craig Venter Institute (JCVI), its predecessors, such as the now-defunct Institute of Genomic Research, as well as the company Synthetic Genomics Inc.[144] The J. Craig Venter Institute began applying for patents for their research in 2006, with the applications covering 13 groupings of patents, including patents relating to the synthesis of genomes and genome fragments.[145] In addition to JCVI and its affiliates, other companies active in SynBio development have also adopted an aggressive stance in pursuing patent protection, such as Sangamo BioSciences, who own the patent[146] to certain methods pertaining to gene switches.[147] Several universities also hold patents on synthetic biology technologies, among which are inventions which may be considered foundational for various approaches within the field.[148] As illustrated by the examples above, the IP frame highlights the patenting of upstream technologies, resulting in subsequent innovation being at least partially dependent on acquiring licenses to such foundational patents.

The A2K model consists of several different organizations and institutions, four of which will be described. The BioBricks Foundation is one of the pre-eminent advocates of the A2K approach in synthetic biology. The Foundation has sought to foster the development and adoption of a shared assembly standard for synthetic biology, the BioBrick™, originally developed by Tom Knight in 2003.[149] The primary purpose of the standard is to ensure the modularity of bioparts, so that developers of new parts can be reasonably certain that their parts can be successfully combined with other existing parts.[150] The essence of the BioBrick standard consist of each biopart ending with recognition sites for a specific set of three restriction enzymes. The biological processes of digestion and ligation at these sites connects

[143] Calvert 2012, p. 174.
[144] van den Belt 2014, p. 31–33.
[145] Chan & Sulston 2010, p. 1.
[146] Patent US 6794136 B1: Iterative optimization in the design of binding proteins.
[147] Kumar & Rai 2007, p. 1754–1755.
[148] *Idem.* p. 1752.
[149] Baldwin et al. 2015, p. 47.
[150] See: BioBricks Standard Assembly webpage.

BioBricks to each other in a standardized way.[151] The BioBricks Foundation operates its own registry for BioBricks, to which anyone may freely contribute resources[152] and conversely, utilize the resources added to this registry[153]. Such actions must conform to the BioBricks Public Agreement, which requires that both the users and contributors commit not to assert any patents, copyrights or data rights against the Foundation or any other users.[154]

The BioBricks Foundation operates in close contact with the International Genetically Engineered Machine (iGEM) competition. The iGEM competition is considered to be one of the prime embodiments of the A2K ethos in synthetic biology. The competition is meant as a platform for teams consisting of high-school students, undergraduates and postgraduate students to tackle real-world problems by constructing biodevices and systems from a kit of approximately a thousand BioBricks.[155] iGEM began in the academic year 2003–2004 as an independent activity period project organized by Tom Knight and Drew Endy, which has since grown to include over 200 teams from all parts the world.[156] The bioparts, devices and systems developed during the previous competitions are part of an intellectual commons.[157] This allows for teams in each subsequent iGEM competition to build on the work done by previous teams. Many of the projects developed in the iGEM competition have led to publications in major scientific journals, such as the 2004 development of a bacterial photofilm by University of Texas at Austin resulting in an article in *Nature*.[158]

The BioBricks developed in the iGEM competition are added to the Registry of Standard Biological Parts (SBP Registry)[159], operated by MIT.[160] This registry contains an open source collection of BioBricks of varying functions. In addition to the parts themselves, the registry contains data pertaining to the usage of the bioparts, along with resources for the synthesis and assembly of novel parts, devices, and systems.[161] The economic impact of iGEM and its open-source ideology is best characterized by the fact that in the 2008

[151] Baldwin *et al.* 2016, p. 48.
[152] BioBrick™ Contributor Agreement, section 1.
[153] BioBrick™ User Agreement, section 1.
[154] *Idem.* section 2.1.
[155] Baldwin *et al.* 2016, p. 120.
[156] *Idem.*, p. 119–120.
[157] Van den Belt 2014, p. 30.
[158] Levaskaya et al. 2005, p. 441–442.
[159] *N.B.:* the SBP Registry is not the same as the BioBrick Registry. The former operates primarily as a repository for BioBricks developed in iGEM, whereas the latter contains contributions from various sources.
[160] Bensaude Vincent 2013, p. 370.
[161] *Idem.*

competition alone, 1,500 parts were added to the SBP registry, the mere patenting of which would have cost an estimated 35 million US dollars.[162]

One common critique levied towards both the open source initiatives above is that the parts developed by them are of relatively low quality, with insufficient metadata for the parts to be of use in developing proper scientific or commercial applications.[163] This criticism has led *inter alia* to the creation of the International Open Facility Advancing Biotechnology project (BIOFAB), which is a collaboration between the US National Science Foundation, UC Berkeley and Stanford University that seeks to produce open source library of high-quality standardized bioparts.[164]

2.4.2. Commonalities and peculiarities

It would be easy to overstate the differences between the IP and A2K models. In actual fact, the two models are in broad agreement over a variety of issues regarding SynBio IPRs. First, a shared consensus exists within advocates of both models regarding the patentability of downstream innovations, especially ones that are ripe for commercialization.[165] The second commonality has to do with the shared view that certain aspects of basic SynBio infrastructure should be treated as part of the intellectual commons.[166] The commons advocates claim that all research inputs, i.e. standards of interoperability and performance, design and testing methods, functional and non-functional fragments of DNA, performance data, and chassis, should constitute a commons. Advocates of the IP frame agree on most of these points, except for functional fragments of DNA, performance data, and redesigned chassis, which in varying degrees are considered subject to proprietary IP protection.[167] The major point of contention lies in the patentability of functional fragments of DNA and minimal chassis microbes, which are the central components in the bioparts-approach of constructing synthetic devices and systems.[168] This also explains the choice to concentrate on the issues arising these forms of upstream inventions.

Many scholars have highlighted the fact that the seemingly competing A2K and IP frames might in actual fact be synergistic. Kumar and Rai note that combining the approaches allows

[162] Bennett 2011, p. 14.
[163] Henkel & Maurer 2007, p. 2.
[164] Van den Belt 2014, p. 31.
[165] Wellhausen & Oye 2008, p. 11.
[166] *Idem.* p. 9.
[167] *Idem.*
[168] *Idem.* p. 10.

for proprietary IP to generate an influx of necessary venture capital into the field, while the unpatented space may mitigate some of the economic problems arising within the proprietary approach.[169] Heller and Maurer argue that the production of bioparts through open source is the best solution, but if an open source approach is unable to do so, a proprietary biopart is societally preferable to having no part at all.[170] As indicated by the examples above, the broad consensus among scholars of the field is that optimal levels of innovation require both a proprietary and commons approach. While many of the individual opinions of these scholars offer ample room for critique, such criticism is not possible in this work without expanding its scope considerably. As a result, the general scholarly consensus of the need of both proprietary innovations and A2K for the effective development of downstream development of SynBio applications is assumed as being valid.

2.5. Responsible Reseach and Innovation

Given overarching objective of this thesis is to ensure welfare, an approach that combines proprietary IP with A2K requires that the patenting of both upstream and downstream SynBio inventions is done in a manner that produces socio-economically beneficial outcomes. This can be viewed as an instance of the broader concept of *Responsible Research and Innovation* (RRI). An operational definition of RRI given by von Schomberg is that it is "a transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (ethical) acceptability, sustainability and societal desirability of the innovation proves and its marketable products"[171].

The concept of RRI is a very topical issue in both theoretical discussions on biotechnology patenting as well as actual contemporary IPR policy. As an example of the theoretical discussion; the re-evaluation of the current relationship between innovation and the greater societal good was a key point in the 2013 Manchester Manifesto, which was signed by a multitude of scholars in bioethics, law, and economics, including two Nobel laureates. The Manifesto highlights a multitude of structural issues arising from the current IP paradigm, especially the patent system, which result in fragmentation of IP, restrictive licensing practices, and various forms of increasing transaction costs.[172] The Manifesto argues that these issues lead to the stifling of scientific progress, lower levels of innovation, and most

[169] Kumar & Rai 2007, p. 1768.
[170] Henkel & Maurer 2007, p. 3.
[171] von Schomberg 2013, p. 19.
[172] Manchester Manifesto 2013, p. 4.

importantly for this thesis, decreased societal welfare.[173] It ends with a call to reorganize our existing IP system and practices to better ensure the provision of public benefit and to facilitate scientific progress.[174]

The importance of synthetic biology RRI in European innovation policy is evidenced by the fact that RRI has been adopted as a central facet of the European Union's Horizon 2020 strategy.[175] Biotechnology in general was identified as one of six 'key enabling technologies' (KET) that has the potential of both improving the industrial and innovative capacities of the Union, as well as addressing various societal concerns and enhancing the quality of life.[176] Synthetic biology was listed as the very first subfield of biotechnology (BIOTEC 1) that warranted concentrated research and innovation actions within the Horizon 2020 program.[177]

Based on the discussion above, it is easy to conclude that the necessity of RRI in synthetic biology is not only a matter of opinion, but also an institutional fact. As one of the fundamental purposes of RRI is to improve the quality of life, it is taken as a matter of course that an RRI approach in synthetic biology results in higher levels of aggregate welfare throughout the European Union. This creates an explicit link between the objectives of this thesis and ensuring RRI in synthetic biology. However, ensuring true RRI in relation to proprietary inventions of synthetic biology is not a straightforward matter. Following a similar line of reasoning as the authors of the Manchester Manifesto, Köning et al. highlight several issues in our current patent system relating to SynBio that may result in both societal and economic failures, thus jeopardizing the goals of responsible research and innovation. According to them, the development of RRI in synthetic biology may be hindered by 1) broad patent claims in fundamental parts or techniques, 2) patent thickets, and 3) a concentration of patents.[178] As a result, a further analysis of these questions, as well as other closely related issues, is central for the purposes of this thesis. Before it is possible to delve into this line of questioning in detail, it is necessary to understand the general relationship of synthetic biology inventions and European patent law. Ensuring RRI through providing solutions to the aforementioned issues engendered by SynBio patents forms the basis of the discussion in Chapters 4–6 of this thesis.

[173] *Idem.* p. 4.
[174] *Idem.* p. 6.
[175] Horizon 2020 website (retrieved 7th Dec 2016)
[176] EC KET Biotechnology report 2015, p. 5–6.
[177] *Idem.* p. 12.
[178] König *et al*. 2015, p. 1058.

3. Synthetic biology in European patent law

3.1. European patent law

Seemingly most of the discussions in the literature regarding the compatibility of synthetic biology with European patent law are based on generalized patent theory[179], with relatively few scholars having analyzed the actual implications of *substantive* European patent law on synthetic biology.[180] The purpose of this chapter is to provide some additional analysis to this effect. It also serves as a natural part of the overall aim of this thesis, as any incompatibility of substantive European patent and the technology itself may jeopardize the development of the technology. Identifying such problems is also of obvious importance in constructing an IP framework for synthetic biology.

Article 118(1) of the Treaty on the Functioning of the European Union[181] (TFEU) warrants the creation of a system that ensures uniform protection for IPRs, including patents, throughout the internal market. This requirement and its historical antecedents have resulted in various attempts to harmonize patent protection within the European Union.[182] While patent law has not been exhaustively harmonized in Europe, efforts to do so have resulted in a two-tiered system in which national patent law operates in tandem with a European framework.[183] The most important component in the latter European dimension is the Convention on the Grant of European Patents of 5 October 1973 (the EPC, revised in the year 2000[184]). Article 4 of the EPC mandated the creation of an autonomous patent authority, the European Patent Office (EPO) to oversee the granting of European patents.

A European patent offers a centralized patent prosecution system for all signatory nations of the EPC.[185] However, a patent created in this way does not constitute a unified IPR in all the contracting nations. A European patent must be validated by the national patent authorities of the signatories of the EPC in which the patentee wishes to obtain patent protection for their invention, meaning that a European patent merely provides a unified pathway of patent

[179] See *e.g.*: Selgelid & Evans 2015 *passim*; Koepsell 2014 *passim*; Marchant 2011, *passim.*
[180] *N.B.:* this in no manner implies that such studies do not exist. See *e.g.*: Schneider 2014 *passim*; Fernandez y Brañas 2014, *passim*; Rutz 2009 *passim.*
[181] Treaty on European Union and the Treaty on the Functioning of the European Union (C 326/47)
[182] Waelde *et al.* 2014, p. 373–375.
[183] *Idem.* p. 371–372.
[184] All subsequent references regarding the EPC contained in this thesis refer exclusively the amended version (EPC 2000) of the Convention.
[185] Kur & Dreier 2013, p. 87–88.

prosecution, which ultimately results a bundle of national patents.[186] To this effect, EPC Article 2(2) states that once the European patent has been granted and validated in a given nation, it will be subject to the same conditions as a national patent, unless otherwise stated in the Convention. Among other things, this indicates that if the European patent expires due to non-payment of fees in one of the contracting states for which it has been granted and validated, this does not have any immediate effect on rights granted in other states.[187] The most crucial example of the role of national law for the purposes of this analysis is EPC Article 64(3), which provides that infringing a European patent shall be dealt with in accordance to national law.

Efforts to harmonize the European patent system have gone further. A major development in this respect took place in 2012, when the European parliament voted in favor of Council Regulations (EU) No 1257/2012[188] on the creation of unitary patent protection (Unitary Patent Regulation), and No 1260/2012[189] regarding the translation arrangements necessitated by such a unitary patent system. As the titles of these regulations would suggest, both concern the creation of *unitary patent protection.* According to Article 2(b) and (c) of the Unitary Patent Regulation, unitary patents are a form of European patent granted by the EPO, the granting of which follows the rules and procedures of the EPC. Compared to a traditional European patent, once granted, the unitary patent offers uniform patent protection that covers all the participating Member States, without the need for *inter alia* national validation.[190]

The unitary patent has not quite come into existence yet. Article 18(2) of the Unitary Patent Regulation states that the regulation will come into effect after the ratification of the Agreement on a Unified Patent Court (UPCA)[191]. The Unified Patent Court is a proposed forum that is open to all Member States of the European Union, although institutionally separate from it. As formulated in the UPC Agreement, the UPC provides a single forum for *inter alia* infringement cases (UPCA, Article 32), and revocation proceedings (UPCA Article 65) of European patents, both traditional and unitary (Article 1). In turn, the UPC

[186] Waelde *et al.* 2014, p. 372, para. 10.23.
[187] See *e.g.*: EPO Website, Applying for a Patent: section 8. (Validation), which states "Depending on the relevant national law, the applicant may also have to pay fees by a certain date."
[188] Council Regulation (EU) No 1257/2012 of 31.12.2012 on implementing enhanced cooperation in the area of the creation of unitary patent protection (L 361/1).
[189] Council Regulation (EU) No 1260/2012 of 31.12.2012 implementing enhanced cooperation in the area of the creation of unitary patent protection with regard to the applicable translation arrangements (L 361/89).
[190] Kur & Dreier 2013, p. 66.
[191] Agreement on a Unified Patent Court of 20 June 2013 (C 175/01).

Agreement will become valid when the three conditions listed in the preamble are met.[192] As of 10 March 2017, this process still requires the ratification of the Agreement by Germany and the United Kingdom.[193]

As a result, European patent law will soon consist of three functionally distinct forms of patents: national patents, traditional European patents and unitary European patents. However, the EPC will remain the paramount force of harmonization in substantive patent law. The reason for his is two-fold. First, as stated above, both forms of European patents are granted in accordance to the EPC. Second, the EPC has resulted in the *de facto* harmonization of central elements of substantive patent law, especially regarding the criteria of patentability.[194] Because of its role as a primary source of substantive law throughout Europe, the main emphasis of the following sections of this chapter will be on the EPC and its interpretation. Before it is possible to concentrate on such matters, it is necessary to discuss the role of EU law on the patenting of SynBio inventions.

3.2. Biotechnology in EU law

Despite the fact that European patent law has traditionally been the remit of the EPC and EPO, the European Union has also had some success in harmonizing substantive patent law. Given the subject of this thesis, the most important example of such efforts is Directive 98/44/EC on the legal protection of biotechnological inventions, more commonly known as the *Biotechnology Directive*.[195] The Biotechnology Directive was crucial in ensuring a unified European approach to various contentious issues that naturally arise from construing the substance matter of all life as a form of property.[196] The criteria for patenting biotechnological inventions are contained in Article 3 of the Biotechnology Directive, which states that:

> *1. For the purposes of this Directive, inventions which are new, which involve an inventive step and which are susceptible of industrial application shall be patentable even if they concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used.*

[192] UPC Agreement (English version), p. 6, *para.* 15.
[193] UPC Ratification Details (EC) webpage.
[194] See *e.g.*: Kur & Dreier 2013, p. 88; Ellyne 2013, p. 147.
[195] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions (L 213/13).
[196] See *e.g.*: Stazi p. 192–195 for a description of the varying views of EU Member states regarding the Directive and its implications.

2. Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature.

Article 2 of the Biotechnology Directive defines biological material as any material containing genetic information and capable of reproducing itself or being reproduced in a biological system. Given the definition of bioparts, devices, systems and chassis provided in section 2.1.2. of this thesis, it is clear that these SynBio components are biological material as meant in the Directive, which also results in their general classifiability as inventions.

The Biotechnology Directive has important implications regarding the upstream inventions used in the creation of bioparts. As stated previously, bioparts often consist of modified forms of naturally existing DNA. As implied by Article 3(2), these naturally occurring sequences, if *isolated*, are considered patentable subject matter. The specific meaning of the word 'isolated' may be derived from Recital 21 of the preamble, in which the isolation of a naturally occurring element implies some form of "technical processes used to identify, purify and classify it and to reproduce it outside the human body, techniques which human beings alone are capable of putting into practice and which nature is incapable of accomplishing by itself".[197] This legislative approach allowing the patenting of isolated but naturally occurring genes of the human body caused a great furor during its legislative process and afterwards[198], leading *inter alia* to the Court of Justice of the European Union (ECJ) case *The Kingdom of the Netherlands v. European parliament and Council*[199]*,* which was set off by the Netherlands requested the annulment of the entire Directive by the Court.[200] The ECJ did not accept the line of argumentation, viewing that sufficient safeguards of human dignity were in place.[201] The approach adopted by the European legislator and ECJ can be contrasted with the US Supreme Court (SCOTUS) 2013 ruling in the case *Myriad v. Association of Molecular Pathology*, in which the court ruled that naturally occurring sequences of DNA constitute non-patentable subject matter even if

[197] See *e.g.*: *Idem.* p. 210–213 for a more thorough discussion on the topic.
[198] *Idem.* p. 192–193.
[199] ECJ Netherlands v Parliament and Council (C-377/98), Judgment of the Court of 9 October 2001.
[200] Application for annulment of Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions (OJ 1998 L 213); p. 13.
[201] ECJ Netherlands v Parliament and Council, para. 77.

isolated, although confirming the patentability of altered sequences of DNA, such as cDNA, as well as applications based on the knowledge of naturally occurring DNA.[202]

Multiple patents have been granted for isolated natural genetic sequences in Europe.[203] This raises the question of the effects of such patents on developing modified variants of gene sequences contained within the claims, such as is often done when designing new bioparts. A similar question applies to the relationship of patented bioparts in devices, patented devices in systems, *et cetera.* The crux of the matter can be boiled down the following three questions: 1) if based on a previously patented gene, how much does a biopart have to be modified in order for it to constitute an invention? 3) How far does the patent protection of a genetic sequence (e.g. a biopart) extend when combined into a system 2) When designing and constructing any such SynBio invention, can a SynBio innovator modify a patented gene or any combination thereof without the need to obtain a license for said patent(s), provided that the resulting biopart is sufficient different from the patented gene?

The first question is partially answered within the preamble of the Directive, although not in a conclusive manner. Recital 25 provides that if a given genetic sequence overlaps with a patented one in a way which is not *essential to the invention*, the former sequence is to be considered as being independent of the latter in terms of patent law. Nowhere in the Directive nor its preparatory works is this criterion of essentiality explicitly clarified; Schertenlieb calls it "an unknown function"[204]. This issue is further compounded by recitals 22 and 23, the first of which states that the *industrial application* of a genetic sequence or partial sequence must be disclosed in the patent application. Recital 23 in turn states that DNA sequence without an indicated *function* contains no technical information, resulting in such sequences being unpatentable. However, the literature indicates that the function of a gene or gene fragment consists of its industrial applicability as disclosed in the patent application, whereas the essentiality of a section of a sequence to an invention is determined by its disclosed function.[205] This allows the formulation of an answer to the first question: the modifications made must result in the biopart having a clearly identifiable function distinct from its patented input, although functionally irrelevant overlap can be safely ignored.

The second question is partially addressed in the Directive itself, with Article 9 providing:

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[202] Supreme Court of the United States of America, case No. 12–398: *Association of Molecular Pathology v. Myriad Genetics, Inc.,* of 13 June 2013, p. 10–18.
[203] See *e.g.*: Verbeure *et al.* 2006, *passim.*
[204] Schertenlieb 2003, p. 12.
[205] See *e.g.*: Díaz Pozo 2017, p. 113.

> *The protection conferred by a patent on a product containing or consisting of genetic information shall extend to all material, save as provided in Article 5(1)*[206]*, in which the product is incorporated and in which the genetic information is contained and performs its function.*

This provision implies that a patented biopart incorporated in a device[207] maintains its proprietary nature, so long as the part in question 'performs its function'. When does such a gene stop performing its function? The answer to this question was at the heart of the ECJ 2010 judgement on the case *Monsanto Technology LLC v Cefetra and Others*. In its judgement, the ECJ determined that patent rights to certain proprietary EPSPS genes that generate a resistance to herbicide 'Roundup' in soy plants do not extend to the end products generated by that plant in which the gene no longer serves a function[208], which in this specific instance was imported soy meal that contained the gene.[209] Taken together, the aforementioned Article 9 and ECJ ruling indicate that the patent protection on a biopart extends all the way to the synthetic microbe that contains it. As stated above, the function is fundamentally determined by the disclosure of industrial applicability.

A key element in answering the third question lies in so-called *experimental use exemptions*, which broadly stated provide a form of 'safe harbor' for scientific research.[210] Such exemptions have been adopted in certain elements of EU law, such as in Article 3(2–3) in Directive 2001/82/EC[211] concerning veterinary medicinal products and 2001/83/EC[212] concerning human medicinal products, but current EU law does not prove a blanket solution for biotechnological patents.[213] This is subject to change, as the Article 27(b) of the UPC Agreement states that patent rights do not apply to acts done for experimental purposes relating to the subject matter of the patented invention. As research exemptions have previously fallen within the scope of national law, resulting in varying solutions throughout Europe, it is unclear what this provision will entail in practice.[214]

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[206] *N.B:* Article 5(1) limits the patentability of the human body and mere discoveries of human genes.
[207] *N.B.:* Or following the hierarchy: a biodevice in a system or a system in a chassis.
[208] ECJ *Monsanto Technology LLC v Cefetra and Others* (C-428/08), Dispute, p. I 6798–6799, para. 15–21.
[209] *Idem.* Ruling, point 1, p. I 6814.
[210] Kur & Dreier 2013, p. 119–120.
[211] Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001, on the Community code relating to veterinary medicinal products (L311/1).
[212] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001, on the Community code relating to medicinal products for human use (L 311/67), as amended by Directive 2004/27/EC of 31 March 2004 (L 136/34).
[213] Kupecz *et al.* 2015, p. 710.
[214] *Idem.* p. 715.

3.3. Patentable subject matter in the EPC

The focus of this section will be on studying the potential issues raised when applying for a European patent for a SynBio invention. This requires an understanding of the criteria of patentability as detailed in Articles 52 and 53 of the EPC, as well as instances of relevant case law of the EPO Boards of Appeal. The first step in such a process is determining whether SynBio inventions generally are patentable subject-matter. This is not an entirely trivial question, as if one was to frame synthetic biology as a form of biological software as suggested in section 2.2., the answer might very well be no, as the current substantive law of the EPC generally prohibits the patenting of computer programs (EPC Art. 52(1)(c)).[215] After the general case of patentability of SynBio has been established, it is possible to concentrate on specific issues raised in EPO case law that have implications for the development of the technology. To this begin this line of questioning in earnest, Article 52 of the EPC provides that:

(1) *European patents shall be granted for any inventions, in all fields of technology, provided that they are new, involve an inventive step and are susceptible of industrial application.*
(2) *The following in particular shall not be regarded as inventions within the meaning of paragraph 1:*
    (a) *discoveries, scientific theories and mathematical methods;*
    (b) *aesthetic creations;*
    (c) *schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers;*
    (d) *presentations of information.*

The concept of technology neutrality contained in Article 52(1) ("for any inventions, in all fields of technology") indicates that inventions of synthetic biology should be considered patentable, provided that they are 1) novel, 2) non-obvious, and 3) industrially applicable. It is also crucial to note that the aforementioned Biotechnology Directive and its interpretations have had a major impact on the substantive law of the EPC. The Directive led to changes in the Implementing Regulations of the EPC, resulting in the implementation of the central provisions of the Directive as Part II, Chapter V of the Implementing Regulations.[216] Rule 26(1) of said Regulations specifies the relationship between the Implementing Regulations,

[215] See e.g.: Hilty & Geiger 2011, p. 161–171 for a detailed discussion on the general topic.
[216] Kur & Dreier 2013, p. 125.

the EPC, and the Biotechnology Directive. It states that the regular rules of patentability in the EPC will be applied and interpreted in accordance to Part II, Chapter V of the Regulations, with the Biotechnology Directive being a supplemental source for interpretation.

In determining what constitutes a biotechnological invention, the EPC has adopted the definitions contained within the Biotechnology Directive.[217] Rule 26(1) of the Implementing Regulations defines biotechnological inventions as inventions which concern a product consisting of or containing biological material or a process by means of which biological material is produced, processed or used. Rule 26(2) defines biological material as any material containing genetic information and capable of being reproduced in a biological system. Rule 26(6) defines a microbiological process as any process involving or performed upon or resulting in microbiological material. Given the definitions above, it can be safely stated that all of the elements contained in the bioparts approach can be construed as biotechnological inventions within the EPC system, as they consist of and produce biological material.[218] In turn, that biological material is capable of being reproduced in a biological system, i.e. the chassis.[219] As the chassis is typically a prokaryote, such as a modified variant of *E. coli* or *S. cerevisiae*[220], any synthetic biology systems that are incorporated into such a chassis are necessarily microbiological processes as well.

Prima facie it would seem that all the main components of the bioparts based approach of synthetic biology meet the criteria of biological inventions, consequently fitting the first requirements of patentable subject matter as meant by Article 52 of the EPC. Studies conducted by *inter alia* Rutz[221] and Fernandez y Brañas[222] also bear out this initial assumption: the EPO considers SynBio inventions patentable. It is now possible to examine the implications of the substantive law on the criteria of novelty, inventive step and industrial applicability on synthetic biology. As stated above, the following section specifically seeks to highlight potential problems that the established forms of interpreting the EPC might engender in synthetic biology.

[217] *Idem.* p. 125.
[218] See: Section 3.2. of this thesis.
[219] *Idem.*
[220] Baldwin *et al.* 2015, p. 43.
[221] Rutz 2009, *passim.*
[222] Fernandez y Brañas 2014 *passim,* arriving at this conclusion in p. 197-198.

3.3.1. Novelty

The general rule of evaluating novelty in the EPC can be found in Article 54, which states the following:

(1) An invention shall be considered to be new if it does not form part of the state of the art.

(2) The state of the art shall be held to comprise everything made available to the public by means of a written or oral description, by use, or in any other way, before the date of filing of the European patent application.

The first step is determining novelty is to define what state of the art or *prior art* means in a given situation, followed by determining what part of the prior art is relevant and what the relevant part contains. After the prior art has been defined, the second step is to compare the new invention to aforementioned prior art. If they differ, the invention is considered novel.[223] While seemingly simple, the interpretation of this rule has become more complex in the case law of the EPO Boards of Appeal, which has some implications as to the patentability of SynBio inventions. The problem arises when trying to determine the scope of the state of the art in relation to knowledge that is not explicitly contained within the art, but that is to some extent implied by it.

The established case law of the EPO Boards of Appeal state that an invention lacks novelty if its subject-matter is can be unambiguously and directly derived from prior art.[224] In the case *T 179/01 (Herbicide resistant plants/MONSANTO)*, the Technical Board of Appeal had to evaluate the implied relationship between DNA and proteins. In the case, the appellants argued that a prior publication indicating the likely relationship of a gene with a *B. subtilis* equivalent of an EPSPS protein destroyed the novelty of the isolated gene sequence claimed by the proprietor of the patent.[225] As the central dogma of molecular biology states: DNA is transcripted into strands of mRNA, which contains the codons that are subsequently translated into proteins by tRNA and ribosomes.[226] If read backwards, the aforementioned process means that if the primary structure of a protein is known, it is possible to infer the

[223] EPO Case Law 2016, p. 69.
[224] EPO Case Law 2016, p. 102.
[225] EPO Technical Board of Appeal T 179/01 (Herbicide resistant plants/MONSANTO), Summary, XI, p. 11–12.
[226] Crick 1958, p. 153.

sequence of the mRNA that encoded it, as well as that of the underlying exonal DNA.[227] This lead the board to consider the possibility of an "indirect proof of inherency", in which knowledge of the structure of one molecule may still destroy the novelty of another molecule, despite the fact that they are structurally entirely dissimilar.[228] The Board came to the conclusion that indirect proof of inherency is sufficient to remove novelty if the prior art provides "a clear, unambiguous and enabling lead to the inherent properties"[229] of the patented genetic sequence or protein.

This conclusion is important for the development of synthetic biology. If the structure of an entirely novel biopart may be clearly and unambiguously deduced from the prior art knowledge regarding the proteins it produces or the structure of existing metabolic pathways, it may imply that a large portion of any biopart is considered state of the art. This may possibly generate some strict boundary conditions for the patentability of simple bioparts.

3.3.2. Inventive step

Article 56 of the EPC states the following:

> *An invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art.*

In evaluating whether an invention is non-obvious, the EPO has adopted a three-point problem-and-solution approach, which consists of: 1) determining the 'closest prior art', 2) determining the nature of the 'objective technical problem' that the claimed invention seeks to solve, 3) Determining whether the purported invention, starting from the closest prior art and the objective technical problem, would have been obvious to the skilled person.[230][231]

The modular nature of bioparts raises an important question in relation to the third point in the problem-and-solution approach. As exemplified by the Artemisin research conducted by Ro et al., synthetic biologists often seek to develop new processes for the production of existing pharmaceutical compounds and biopharmaceuticals.[232] If natural processes for the

[227] *N.B.:* mRNA may contain 64 different codons, but they only translate to 22 amino acids, meaning that the process of backward deduction is limited. As an example, leucine is encoded by six different codons, meaning that six possible variations of DNA result in the same protein. See e.g.: Glick *et al.* 2010, p. 30.
[228] T 179/01, Reasons, point 12; p. 20.
[229] T 179/01, Reasons, point 13; p. 20–21.
[230] EPO Guidelines, Part G-VII, para. 5.
[231] *N.B.:* EPO Guidelines, Part G, Chapter VIII, paragraph 3, defines a 'skilled person' as "a skilled practitioner in the relevant technology, possessing average knowledge and ability, and knowledgeable of the state of the art in that field".
[232] See *e.g.*: van den Belt 2014, p. 3–4.

production of such compounds already exist, would their synthetic emulation entail some level of obviousness? In its case T 2/83, the EPO Technical Board of Appeal stated that a course of action may be deemed obvious pursuant to Article 56 if a skilled person would have taken that action while expecting an advantage or improvement as result of it.[233] This point was further clarified in T 0149/93, which explicitly stated that while a clearly predictable course of action is obvious, a *reasonable expectation of success* may render a purported invention obvious as well.[234] Consequently, if a synthetic biopart emulates nature too closely, such as being a modularized version of a prior art gene constructed using a pre-existing standards, it is likely to be considered obvious.

However, the latter ruling raises another point: if the modular gene sequences responsible for the production of those compounds are considered prior art, would combining them and adding them into a chassis be considered obvious? This problem can be generalized to all bioparts. If the assembly of bioparts seeks to replicate some well-known process and the bioparts used are sufficiently modular, it implies that constructing a system or device based on those parts is relatively straightforward for the skilled person. In this vein, scholars, although grossly simplifying the matter, have compared bioparts and their assembly into devices to assembling Lego bricks.[235] This may potentially result in situations in which downstream commercial applications are unpatentable by virtue of being obvious. In such a situation, upstream innovators would be incentivized to seek strong IPR protections at the level where they are likely to obtain them. This would logically make the patenting of bioparts more enticing, resulting in the solidification of upstream patenting as a necessary practice to recoup R&D costs. This could potentially exacerbate the problems faced by synthetic biology. Therefore it is imperative to design a solution for such a problem.

The issue seems to hang on what can be defined as a "reasonable expectation of success". The general outlines can be determined from the following five cases. In case *T 2168/11*, the Board made a general delineation based on its existing case law[236] that the standard is not one of absolute certainty.[237] The fact that other competing research teams were all following a similar course of action might indicate that that approach might be obvious to try, but in *T 296/93*, the Board specifically stated that such hopes of success do not entail obviousness

[233] EPO Technical Board of Appeal, Decision: T 2/83 (Simethicone Tablet/Rider); Reasons, point 7.
[234] EPO Technical Board of Appeal, Decision: T 0149/93 (RETINOIDS/Kligman II); Reasons, point 5.2.
[235] See *e.g.*: Anderson et al. 2012, p. 586; Robienski & Simon 2014, p. 130.
[236] Specifically referring to cases T 192/06, T 278/03, and T 918/01.
[237] EPO Technical Board of Appeal, T 2168/11 (Alzheimer's disease beta amyloid peptide mouse model/ELAN ELI); Reasons, point 11, p. 32.

through a reasonable expectation of success. After all, any amount of such endeavors might end up failing. The Board continues by offering the following definition of a reasonable expectation of success: it is at hand when the skilled person is able to rationally foresee, based on knowledge existing prior to the commencement of a research project, the success of the project within a reasonable time frame. This implies a criterion of proportionality, in which expectations of success are deemed to be lower in new fields of technical research.[238] In cases T 816/90 and T 923/92 the Board iterated a position in which a theoretically straightforward course of action resulting in the solution does not necessarily imply a reasonable expectation of success, as the latter requires the ability to reliably make valid decisions when faced with complications.[239] Finally, in case T 207/94 the Technical Board of Appeal stated that allegations targeting reasonable expectation of success must be based on technical facts.[240]

Based on the jurisprudence of the EPO Boards of Appeal, it is possible to construct a generalized understanding on how the criterion of reasonable expectation of success is likely to affect bioparts and their assembly. As it currently stands, most new applications of bioparts require the construction of a new metabolic pathways, which is currently far from a trivial endeavor.[241] Taking into account the nascent stage of the technology and the metabolic complications that constantly plague attempts to construct useful modular biosystems[242], it is unlikely that allegations of obviousness based on a reasonable expectation of success will be accepted by the EPO.

This may change in the future if structurally and functionally new bioparts utilize existing or similar metabolic pathways as older ones. The success of the field is in fact somewhat reliant on that happening.[243] If we assume that assembling bioparts into systems becomes sufficiently easy, the criterion of 'reasonable expectation of success' may *in extremis* preclude the patenting of downstream applications resulting from such a process, or at least significantly reduce the potential scope of patent claims. This can result in seeking patents further upstream, as the creation of new bioparts and chassis will presumably continue to

[238] EPO Technical Board of Appeal, T 296/93 (HBV antigen production/BIOGEN INC), Reasons, point 7.4.4.
[239] EPO Technical Board of Appeal, T 816/90 (CHB II/ALKO); Reasons, point 5.2.7, p. 9–10. T 923/92 (human t-PA/GENENTECH); Conclusions, point 57, p. 53–54.
[240] T 207/94, OJ 1999, 273 (Human beta-interferon/BIOGEN); Headnote.
[241] Yadav *et al.* 2012, *passim.*
[242] See e.g.: Kuk Lee *et al.* 2008, *passim.*
[243] Henkel & Maurer 2007, p. 1.

have a much lower expectation of success than their subsequent assembly.[244] More importantly, no matter how simple the scientific process of assembling bioparts into systems becomes, the existence of such upstream patents means that commercialized downstream biosystems will require at least some patented technologies as inputs. Obtaining the necessary licenses means that developing novel downstream applications of synthetic biology will remain a costly endeavor, but with the additional detriment of a decreased scope of patent protection for the commercial application itself. This generates an obvious incentive problem, the solving of which will be discussed in chapter 6.

3.3.3. Industrial applicability

The final step in assessing the four criteria of patentability as they pertain to synthetic biology involves industrial applicability. To wit, EPC Article 57 provides:

> *An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture.*

As a starting point for the interpretation of this provision, Rule 29(3) of the Implementing Regulations specifies the nature of the Article above in relation to genetic sequences and partial sequences by stating that the industrial application of any such invention must be specified in the patent application. Guideline G-III, 4. contains the specific disclosure requirements. Following similar provisions as in recitals 23-25 of the Biotechnology Directive, the rule specifies that in the case of exons, the encoded protein must be disclosed, or if the sequence is non-exonal, its function must be described in some other manner.[245] In concordance with Recital 23 of the Biotechnology Directive, Rule 29(3) additionally specifies that applications for genetic sequences that do not contain a specified function for the sequence do not fulfil this criterion. In effect, this rule effectively "raises the bar", precluding the speculative patenting of genetic material.[246]

The question of industrial application is generally considered to be of relatively minor consequence, save for the requirements of disclosure outlined above.[247] However, one specific case is worthy of note in this discussion. In case T 0870/04, the TBA was tasked

[244] *N.B.:* To make a very simplistic analogy: LEGO bricks were considered patentable subject matter (U.S. patent US3005282 (A)), but a tower made of such bricks would certainly not be, even if such a tower had some interesting commercial application.
[245] *N.B.:* This rule is follows recital 24 of the Biotechnology Directive almost *verbatim*.
[246] Díaz Pozo 2017, p. 130–131.
[247] *Idem.* p. 82.

with evaluating an appeal pertaining to a rejected patent application claiming the structure of the protein BPD1 and production methods thereof.[248] The application was rejected *inter alia* due to the fact that it only contained indications of prospective industrial use that was contingent on future development of the field.[249] The Board concluded that speculative industrial application is insufficient, with the application leaving its reader the burden of having "to guess or find a way to exploit it in industry by carrying out work in search for some practical application geared to financial gain, without any confidence that any practical application exists"[250]. In effect, this means that merely describing a protein as indicated by Guideline G-III, 4 does not ensure industrial applicability, nor is it sufficient to have that protein be in some way useful as an object of basic research.

Due to the design element inherent in the modularity of bioparts, it can be assumed that no sensible research effort will be expended in studying or constructing parts with no function. Therefore it is likely that a description of the role of the part in a device or a device in a system is sufficient to fulfil the requirement of industrial application. However, the case T0870/04 does have implications to the basic research from which synthetic biology derives its materials. In that field, mere indications and possibilities of industrial application are insufficient. This can be construed as being positive for SynBio, as it results in certain products of fundamental research being unpatentable, lowering the amount of patent inputs required in constructing e.g. a biopart.

3.3.4. Ordre public

One final issue of patentability remains, which involves the general rules that denote *non-patentable subject matter*. Most patent legislation worldwide contains a prohibition against granting patents to inventions against that are against general public morality, i.e. *ordre public*. Article 53(a) contains the following provision on the matter:

> *European patents shall not be granted in respect of:*
>
> *(a) Inventions the commercial exploitation of which would be contrary to "ordre public" or morality; such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States.*

[248] EPO Technical Board of Appeal, T 0870/04 (BDP1 Phosphatase/MAX-PLANCK) of 11.5.2005.
[249] T 0870/04, Reasons, points 18–23, p. 19–21.
[250] T 0870/04, Reasons, point 19, p. 19.

Many commentators have argued against such considerations in the patenting process, as well as the inclusion of an ordre public provision in general.[251] The primary argument in this view is that granting a patent is not the same as granting approval to produce the invention specified by the patent.[252] As an example, synthetic biology inventions must comply with a wide range of other regulation.[253] Accordingly, the most natural place for moral and ethical considerations is in authorization and compliance procedures created through other legislation and regulation. The patent authority should only consider whether the patent application fulfils the traditional criteria of patentability[254], namely whether the purported invention is novel, inventive, and industrially applicable.

Other scholars choose to take a diametrically opposing view on the matter. In the case of biotechnological patents, and synthetic biology by extension, scholars such as Schneider have discussed the idea of expanding the scope of Article 53(a) of the EPC by allowing the consideration the broader societal consequences of SynBio patents. In this model, the ordre public considerations would include bioethical evaluation, such as the patents' implications to public health, biodiversity, and the availability of nutrition, as well as purely economic ones, such as considering the patent's effects on the concentration of economic power and possible market failures that may arise from such a process.[255] In effect, this can be seen as an attempt at including aspects of RRI as discussed in section 2.5. of this thesis into the criteria of patentability.

Both the arguments certainly have their merits. The opponents are undoubtedly correct that in most situations, it is the commercialization and usage of the invention itself that can be detrimental, and the regulatory authorities have sufficient means to deal with such issues. This point of view is predicated on managing the negative consequences of the patented inventions. However, the scholars opposing ordre public arguments seemingly fail to note the potential negative consequences of the *patents themselves*. As stated previously, the granting of exclusionary rights entails a monopoly, which can potentially be extremely

[251] See *e.g.*: Brody 2007, p. 90.
[252] Ottolia 2011 p. 326.
[253] Regarding the subject matter of this thesis, the most pertinent example of such regulation is Regulation EC 726/2004, which creates a compulsory centralized authorization scheme for medicinal products manufactured by recombinant DNA technology (see Annex 1 of regulation). This includes many applications of synthetic biology. Depending on the specific nature of the SynBio invention, other regulations will apply, e.g. Directives 2001/18/EC and Regulation (EC) 1830/2003, both of which pertain to GMO risk. management.
[254] Ottolia 2011, p. 326.
[255] Schneider 2014, p. 153.

detrimental both in terms of static and dynamic efficiency. This theoretical discussion on ordre public leads us to the following question: does the EPO consider the socioeconomic issues raised by patents as an element of ordre public? If so, some of the potentially negative effects of upstream patenting on SynBio innovation could be taken into account in the patenting process.

In its decision G1/98[256], EPO's Enlarged Board of Appeal (EBA) formulated a clear response to the relationship of economic consequences and ordre public. The patent in question related to a plant product produced through rDNA technology[257]. In the decision, the EBA concluded that its task was not to evaluate the economic consequences of patents in specific areas, or to restrict the scope of patentable subject-matter as a result of such evaluations.[258] The Board continues by stating that biotechnological inventions are not considered to be contrary to public morality in the Contracting States even in an economic sense, as the Biotechnology Directive establishes the necessity of promoting innovation in this field in Europe.[259]

This issue was further discussed in the decision T 1213/05[260]. The case in question revolves around the patentability of a tumor suppressor gene, BRCA1. Certain mutations in BRCA1 are highly correlated with a susceptibility to breast and ovarian cancer in women[261], which results in its high relevance in genetic screening tests provided to women with a familial history of those forms of cancer. In the case in question, one of the opponents (Greenpeace) argued that EPO's Technical Board of Appeal should consider the applicability of Article 53(a) in determining the patentability of BRCA1. Greenpeace argued that the patent in suit would have negative socio-economic consequences by increasing healthcare costs, as well as limiting research and diagnosis modalities, all of which would be highly detrimental to carriers of the gene and doctors alike.[262] The Technical Board responded by noting that Article 53(a) in general pertains only to the effects of the commercial exploitation of the *invention*, not the *patent*.[263] Greenpeace attempted to qualify this statement by noting that

[256] EPO Enlarged Board of Appeal G1/98, (Transgenic plant/NOVARTIS II) of 20.12.1999.
[257] EP 0448511 A1, Anti-pathogenically effective compositions comprising lytic peptides and hydrolytic enzymes
[258] G1/98, OJ EPO 2000, 111; point 3.9, p. 27.
[259] G1/98, OJ EPO 2000, 111; point 3.9, p. 27.
[260] T 1213/05 (Breast and ovarian cancer/UNIVERSITY OF UTAH)
[261] Miki *et al.* 1994, p. 66.
[262] T 1213/05, point 52, p. 49–50.
[263] T 1213/05, point 53., para. 3–4, p. 50–51 (italics added).

the patent and invention were inseparable in this case.[264] This argument was rejected by the Technical Board. The Board went on to state that as patents generally limit competition, such an objection could be made for any patent in any field.[265] As the EPC does not contain any basis for discriminating between patents in this manner, the ordre public-argument cannot be used to render otherwise patentable subject-matter unpatentable in this way[266].

In summation, EPO's stance on the matter is clear. Negative socioeconomic consequences cannot be construed as rendering an invention unpatentable as meant in Article 53(a). Even if such arguments were possible, they would have to pertain to the exploitation of the invention, not the patent itself. Consequently, such concerns cannot be used to mitigate patent-economic problems. Some criticism of EPO's argumentation is however warranted. The argument in case G1/98 of the Biotechnology Directive establishing the economic necessity of patenting biotechnological inventions does not attest to the welfare effects of such patents. It makes sense as a purely *positivist* argument, but the wording of the decision indicates that the reference establishes an *economic fact* by means of legislation.

3.4. The patent landscape of SynBio

As a final note on this chapter of substantive patent law, it is necessary to include some concept of the actual patent landscape of synthetic biology inventions in Europe. Due to the proximity of SynBio and rDNA technologies, it is very difficult to formulate a clear picture on the patent landscape of synthetic biology. A patent analysis study by van Doren et al. indicates that up to the year 2010, 1,195 WIPO patents have been granted for inventions involving synthetic biology, with a total of 3,998 applicants involved in said applications.[267] The analysis also indicates that most of the activity in filing patents took place in the United States of America, with Japan and Germany following.[268] The global trend is one of increasing patent activity, increasing from only 8 filed patents *per annum* in 1991 to 86 in 2010.[269] However, as there is no IPC subclass or subgroup for synthetic biology, the authors acknowledge that their choice of search terms will likely have limited the scope of the search.[270]

[264] T1213/05, point 55, Recitals J, L, 4, and 5., p. 52–53.
[265] T1213/05, point (53), para 6–8.
[266] Fernandez y Brañas 2014, p. 193.
[267] Van Doren et al. 2013, p. 215.
[268] *Idem.*
[269] *Idem.*
[270] *Idem.* p. 219

4. The IP economics of synthetic biology

4.1. The economic rationale of patents

As is likely clear by this point, the IPR of choice in synthetic biology is patenting. Given the general nature of the preceding allusions regarding the potential of patents to generate socio-economically suboptimal results[271], a more rigorous analysis is necessary in to form a clear view on the matter. As the objective of this thesis is to maximize aggregate welfare through ensuring the viability of synthetic biology, the most natural language for such a further analysis is economics. Building on a coherent understanding of the fundamental economic logic of the patent system and its objectives allows us to highlight the specific socio-economic issues that synthetic biology might face in the future. Using the same toolkit, it is also possible to identify certain generalized economic solutions. Performing such an analysis is the exact purpose of this chapter. First, it is necessary to understand the nature of the rights that a patent entails and the justifications of such rights.

The primary right entailed by a patent is to provide the patentee with the *temporally limited right to exclude others from using the invention without the permission of the patentee.*[272] This right of exclusion generates what is in effect a monopoly right to the technology in question[273], provided that the use of the invention is not limited by other authorization mechanisms, such as with patented pharmaceutical compounds.[274] The welfare detrimental nature of unrestricted monopolies is generally considered to be an economic fact[275], at least to the extent that legislators view it as one. It is therefore necessary to understand the reasoning of legislators in creating a system that encourages the inefficiencies generated through monopolization.

Machlup and Penrose give a summary of the traditional arguments to justify the existence of a patent system. The first two of the arguments are based on idealistic notions of inalienable property rights[276] and compensatory justice[277]. The following two arguments are economic in nature, and thus are more consequential to the approach adopted in this thesis. The third

[271] See section 2.5. of this thesis.
[272] See *e.g.*: WIPO IP Handbook, p. 17, section 2.3.
[273] See e.g.: Cooter & Ulen 2004, p. 122–123.
[274] *N.B.:* As an example: Article 6(1) of Directive 2001/83/EC provides that medicinal products for human use require marketing authorization before placed on the market, patent protection notwithstanding,
[275] See e.g.: Motta 2004, p. 41–45.
[276] Machlup & Penrose 1950, p. 17.
[277] *Idem.*

argument states that patent systems are the simplest way to ensure that both inventors and investors may attain a profit from their venture, thus creating an incentive for new innovations.[278] The fourth argument is that patent systems ensure the disclosure of new developments in technology, thus ensuring the dissemination of ideas and further spurring innovation.[279] Multitudes of scholars have adopted similar definitions, highlighting the importance of patents in improving welfare by providing a legal monopoly of pre-determined length for innovators to recoup their R&D costs.[280] The essence of this reasoning lies in the notion that while innovation generally improve the market power of the innovator, if the innovator does not have means of appropriating the outcomes of their research, others will freeride on the results, logically leading to either a) keeping innovation as secret as possible, which reduces the overall development of technologies, or b) no innovation at all.[281] This logic highlights the primacy of *dynamic efficiency* concerns over *static inefficiency*, meaning that innovation is deemed to be of greater societal importance than the monopoly pricing entailed by the granting of exclusionary rights.[282]

These traditional views on the economic logic of patents have been built upon considerably since Machlup and Penrose provided their overview. Multiple patent theorists have developed more refined models, most of which generally contain the same line of reasoning as outlined above, but add novel aspects. Two such schools of thought will be considered in the following discussion: *prospect theory* and *anticommons theory.*[283]

4.2. Prospect theory

Prospect theorists emphasize the importance of patents as property rights.[284] While following broadly similar ideas regarding the traditional incentives to invent presented by Machlup and Penrose, prospect theorists focus on the *ex post* role of patents as tools for the optimal management of inventions.[285] Prospect theory builds on two established economic concepts: *tragedy of the commons* and *Coase's theorem.*[286] The first of the two concepts was coined by Garret Hardin in a 1968 article in the journal *Science*, in which he posits that a commons

[278] *Idem.* p. 21
[279] *Idem.* p. 25
[280] See *e.g.*: Motta 2004, p. 65.
[281] *Idem.* p. 57–66.
[282] *N.B:* For a discussion and definition on these forms of efficiency, see Appendix 1, section II.
[283] *N.B.:* Other theories include Arrow's *theory of competitive innovation* and Merges & Nelson's *theory of cumulative innovation*. For a summary of these theories, see: Burk & Lemley 2003, p. 18–21.
[284] See *e.g.*: Kitch 1977, p. 265.
[285] Burk & Lemley 2003, p. 16–17.
[286] *Idem.*

resource, such as fish in the ocean, is characterized by the lack of any user having the right to exclude others from using that resource, which leads to that resource being overused.[287] The common solution for the commons problem is to privatize the commons resource, granting property rights which, by definition, include the right to exclude others from using the now-private property.[288] One of the fathers of the prospect theorem, Edmund Kitch, argues that a similar situation exists with innovative ideas if they were to be constructed as non-proprietary public resources; generating commercial applications of those ideas would be very inefficient without the means to make the ideas proprietary.[289] Assigning 'prospect' rights similar to what are used in the mining industry is a way to overcome this problem.[290]

The importance of the second aspect of prospect theory, Coase's theorem, hinges on the fact that patent rights are transferrable and subject to be licensed to others. Coase's theorem states that the initial allocation of property rights does not matter if transaction costs are low and property rights are well defined. In such a situation, the free market will ensure an efficient allocation of property rights through bargaining, which results in a coherent property structure that internalizes economic externalities.[291] In the view of prospect theorists, the assigning of prospect rights to ideas combined with Coasean bargaining ensures that such ideas are turned into commercial products in the most optimal way possible.[292]

Prospect theory by contains an inherently positive attitude towards upstream patenting.[293] Their general point in this respect is that extensive patent rights in the highest points of the upstream, actors within latter two stages of development may easily misappropriate the work and investment of the initial researchers, leading to freeriding and diminished incentives in generating and investing in initial innovations.[294] In second, due to the lack of prior art, patent claims in foundational inventions can be constructed broadly, which is likely to generate significant investment into new fields of technology[295], thus spurring technological advancement and the dynamic efficiency benefits it entails.

[287] Hardin 1968, p. 162.
[288] Burk & Lemley 2003, p. 16–17.
[289] Kitch 1977, p. 271–280.
[290] *Idem, passim.*
[291] Coase 1960, p. 42–44. For the simplified formulation used above, see: Cooter & Ulen 2004, p. 89.
[292] Burk & Lemley 2003, p. 16–17.
[293] Wang 2008, p. 265.
[294] Kieff 2001, p. 724–726.
[295] *Idem.* p. 707–712.

4.3. Anticommons and patent thickets

Since the late 1990s, an increasing amount of study has been devoted to the critique of the prospect theorem and its conclusions. While accepting the fundamental role that patents play in fostering innovation as described by Machlup and Penrose, these critics have sought to illustrate that an increased number of patent applications and grants might in fact be economically, scientifically, and socially welfare-detrimental. In the words of Nobel laureate Joseph Stiglitz:

> "*[W]e have an innovation system in which one innovation builds on another. If you get monopoly rights down at the bottom, you may stifle competition that uses those patents later on, and so . . . the breadth and utilization of patent rights can be used not only to stifle competition, but also [can] have adverse effects in the long run on innovation. We have to strike a balance*."[296]

The critics of prospect theory generally base their argumentation on the following two concepts in patent economics: *the tragedy of the anticommons* and *patent thickets*. As the name would indicate, the tragedy of the anticommons is a conceptual mirror-image the aforementioned commons tragedy. In his seminal article on the topic, Heller sought to illustrate that attempts to fix the tragedy of the commons through privatization can lead to a result which is equally detrimental, namely "*a property regime in which multiple owners hold effective rights of exclusion in a scarce resource*"[297]. The problem in such a situation is that the initial endowment of property is done in a disaggregated manner, which results in multiple owners being able to exclude each other from using the resource in question[298], with no single party having effective privileges of use[299]. Heller argues that the incentive to use exclusionary rights to extract maximal rent results in the wasteful underuse of the resource.[300] An apt analogy for an anticommons is that it is similar to the likely effects of a fictitious constitutional requirement of unanimity in passing legislation. If such a rule existed, a single Member of Parliament voting against a proposal would result in the proposal not passing. Given the nature of democracy, it is likely that someone will always vote against any given proposal, at least if not promised something in return. As it is likely impossible to

[296] Stiglitz 1996, para. 6.
[297] Heller 1998, p. 668.
[298] *Idem.* p. 623.
[299] Heller & Eisenberg 1998, p. 698.
[300] Heller 1998, p. 624.

bribe everyone that can block legislation in every instance, little to no legislation would be passed.

Despite its origins in discussing post-socialist property rights, commentators were quick to point out that the nature of patents as instruments of exclusion results in the patent system having an inbuilt potential to generate anticommons problems.[301] Building on this line of reasoning, Heller and Eisenberg argue that the biotechnological industry has an especially high potential to form anticommons due to the prevalence of large amounts of exclusionary property rights in general[302] and upstream patents in particular[303]. In effect, Heller and Eisenberg argue that biotechnology is a complex technology, which by definition[304] requires multiple complementary innovations in order to generate efficient solutions to technical problems. Innovation in these fields may easily result in property rights to such technical solutions being granted exactly in the manner described by Heller.[305]

4.3.1. Fragmentation and overlap

The fundamental problem in a patent anticommons is one of *fragmentation*. This is a direct result of the increasing number of complementary upstream patents, which logically requires the innovator to obtain multiple licenses from multiple patentees.[306] Fragmentation can occur both vertically and horizontally. Horizontal fragmentation denotes a situation in which upstream patents consist of multiple complementary 'pieces' of technology from the same level of technological development that are in some way combined in the new product.[307] Vertical fragmentation is especially relevant in fields of cumulative innovation. Such fields are vertically fragmented if multiple upstream patents cover the preceding steps in the cumulative process.[308] As applied to synthetic biology, an example of horizontal fragmentation is the need to combine multiple proprietary bioparts into a device, whereas vertical fragmentation is at hand if a SynBio innovator must obtain licenses to research tools, fundamental technologies, bioparts, and devices in order to assemble a novel system.

A very similar problem may arise when two or more patents have claims that overlap, making it exceedingly difficult for a downstream innovator to determine which of the

[301] Waelde *et al.* 2014, p. 454.
[302] Heller & Eisenberg 1998, p. 698
[303] *Idem.* p. 699
[304] See section 2.1. of this thesis.
[305] Shapiro 2001, p. 119.
[306] van Overwalle 2016, p. 4–5.
[307] Burk & Lemley 2003, p. 22.
[308] *Idem.*

patents, if not all, should be licensed.[309] Even if the patent landscape was not particularly fragmented, an innovator might still be required to obtain multiple licenses, as it would be impossible to determine *ex ante* which of the overlapping patents is relevant. Following Burk and Lemley's nomenclature, this phenomenon is referred to as a *patent thicket.*[310][311] Although seemingly similar, the distinction between anticommons and patent thickets is an important one. Fragmentation does not necessarily imply overlap, as the claims contained within the multitudes of upstream patents might be easily distinguished from one another; it is the sheer number of such patents which results in fragmentation. On the other hand, overlap does not automatically entail high levels of fragmentation. If only two upstream patents have overlapping claims, it can hardly be said that the patent landscape is fragmented.[312] The practical importance of this conceptual distinction will be revisited when discussing solutions to these two problems.

Despite their differences, both anticommons and patent thickets entail similar economic problems. Researchers of patent economics have identified three distinct types of market failure that arise from these two concepts: *royalty stacking, patent hold-up* and *suboptimal transaction costs*. Royalty stacking is a result of the complementarity of upstream patents in both anticommons and patent thickets.[313] In both situations, a new innovation requires several patented technologies as inputs, which necessitates that the innovator obtain licenses for all such inputs, assuming that the innovator does not wish to run the risk of a patent infringement suit, including the risk of an injunction on producing the product containing the patented technology.[314] Economic logic based on the most rigorous formulation of the rational choice theorem[315] dictates that the licensors of these input technologies will each seek to maximize the value of their own IP by demanding as high royalties for the license as possible.[316] In doing so, the licensor has no direct reason to take into account the fact that the licensors of other complementary technologies are doing the exact same thing.[317] If a sufficiently large amount of licenses is required, the cost entailed by the royalties may

[309] Shapiro 2001, p. 119–121.
[310] Burk & Lemley 2003, p. 23.
[311] *N.B.*: The literature is extremely inconsistent in its use of the terms 'anticommons' and 'patent thicket', and how fragmentation and overlap relate to them; many scholars use the terms in a seemingly interchangeable fashion.
[312] van Overwalle 2016, p. 6–7.
[313] See *e.g.*: Lemley & Shapiro 2007, *passim* for an extensive discussion on the relationship of Cournot complements and royalty stacking.
[314] *Idem.* p. 1993.
[315] Korobkin & Ulen 2000, p. 1066.
[316] Lemley & Shapiro 2007, p. 1996–1999.
[317] See: *Idem.* p. 1996–2000 for a formal model.

subsume or even exceed the value of the downstream invention, resulting in downstream innovation generally becoming economically unviable.[318] In this sense, royalty stacking is equivalent to the well-known problem in pricing complementary goods identified by Cournot, which states that complementary goods sold by separate monopolists result in lesser demand than if a single monopolist selling both goods.[319]

Patent hold-up is a strategic problem that arises from the blocking nature of proprietary upstream technologies. According to Shapiro, if an innovator has already expended a great amount of resources into a the development of a downstream technology, such as hiring R&D staff, constructing a laboratory, and obtaining other necessary licenses, the economic importance of any remaining blocking patents becomes all the much higher.[320] If the licensor of a remaining blocking technology is aware of the licensee having committed themselves to a project that the licensor has the power to block, the bargaining power of the licensor increases dramatically.[321] In turn, general economic logic states that an increase in bargaining power equates to a higher payoff for the party that has it.[322] Combined with the royalty stacking discussed above, this indicates that the cost of licensing increases for each subsequent blocking technology.[323] The problem of patent hold-up may be exacerbated by the phenomenon known as the *sunk cost fallacy*, in which the licensor does not fully appreciate the fact that the resources expended prior to the licensing cannot be recovered.[324] To put it more simply: the more one has committed themselves to a project, the harder it is to abandon it, and the more someone can charge for making it possible to continue it.

The general problem of *suboptimal transaction costs*[325] is less strategic than either of the aforementioned problems. One instance of fragmentation and overlap increasing transaction costs is the issue of *search costs*, denoting the simple fact that a licensor must locate all the relevant patents that they require as inputs.[326] As an example of extreme fragmentation and search costs, downstream developers in the smartphone industry may require up to 15,000 patented technologies as inputs merely to ensure that their product *conforms to a set of*

[318] *Idem.* p. 2012–2017.
[319] Henkel & Maurer 2007, p. 2.
[320] Shapiro 2001, p. 125.
[321] *Idem.*.
[322] See *e.g.*: Dixit *et al.* 2009, p. 693.
[323]Shapiro 2001, p. 125–126.
[324] See *e.g.*: McAfee *et al.* 2010, p. 323–324 on the general behavioral case of the sunk cost fallacy.
[325] Shapiro 2001, p. 126.
[326] EPO ESAB Report 2015 II, p. 5.

technical standards,[327] let alone the patents on the other components of the phone. The mere act of identifying all such patents requires considerable expenditure of time and effort, especially for new companies in the industry. Exacerbating the issue of search costs is the fact that the patents may be traded, requiring that the patentee either locate the new patent holder/licensor or risk having to adopt an entirely alternate technological approach in developing their product. As it currently stands, the EPO holds no centralized register of patent transactions after the opposition period for the patent has concluded.[328][329]

A second instance of increased transaction costs has to do with the *bargaining costs* of acquiring the licenses. Assuming that the licensing agreements for all upstream patents are not identical, obtaining multiple licenses requires expending a great deal of resources in the actual negotiation and drafting of each individual licensing agreement.[330] The relationship of both these transaction costs to the number upstream patents is linear: the more fragmented and overlapping the field, the more relevant patents must be identified and licensing agreements must be negotiated. If all of the upstream patents are not of extremely high economic importance to their respective patentees, this configuration is likely to be non-Pareto optimal.[331] To clarify this point: if the necessary upstream patents were held by a single entity, a single licensing agreement and the transaction costs it entails would suffice.

Patent economists have noted that if sufficiently compounded, the aforementioned effects can lead to the abandonment of R&D efforts.[332] To ensure the viability of any technology that may exhibit such effects requires some form of solution to fragmentation, overlap and transaction costs. Even though both anticommons and patent thickets have the potential to generate similar market failures, their conceptual difference indicates somewhat different structural remedies. Solving the anticommons requires the aggregation of patent rights into a coherent whole, whereas solving the patent thicket requires narrowing the scope of patent claims to reduce overlap.[333] It must be noted that some scholars argue that the aggregation of upstream patents is patent pools is a viable way to deal with patent thickets and overlap

[327] EPO ESAB Report 2012, p. 9.
[328] EPC Implementing Regulations 22–24 and 85 limit the period to opposition proceedings following the grant of the patent. See also: EPO National Law Relating to the EPC, section IX.
[329] *N.B.:* This is subject to change after the adoption of the unitary patent system, as Article 2(e) of the UP Regulation provides that the European Patent Register will contain all such information regarding unitary patents.
[330] Cooter & Ulen 2004, p. 220.
[331] See *e.g.*: Demsetz 1968, p. 61.
[332] See *e.g.*: Buchanan & Yoon 2000 p. 9–10 for a formal mathematical model of the R&D stifling effects generated by an increasing number of exclusionary rights holders.
[333] Van Overwalle 2016, p. 6.

as well.[334] Following van Overwalle's argumentation and the approach adopted by the EPO[335] leads to the conclusion that this is not the case. Even though aggregation may reduce the effect of overlap, this approach to solving the patent thicket does not take into account the possibility that a future overlapping technology might emerge.[336] Even if all the pre-existing overlapping technologies were aggregated, the patentee of a new overlapping technology would potentially be able to demand royalties or sue the licensees of the bundle for patent infringement.[337] Consequently, the only structural solution to patent thickets is to ensure that patent claims do not overlap.

4.4. Prospects vs. anticommons in biotechnology and synthetic biology

The fundamental incompatibility of the prospect model and the anticommons model in regards to the patenting of upstream inventions has resulted in a lively debate between proponents of each model. Compounding the issue is the original formal model that compares the two, which shows that both commons and anticommons are conceptually symmetric, thus assuming an equal deadweight loss in welfare in both situations.[338] As prospect theory addresses the former and anticommons the latter, this would imply that there is no effective way to choose between the two theories of patent protection, as both lead to similar levels of socioeconomic loss. However, further economic modelling has shown that as the transaction costs entailed in the generation of an anticommons are asymmetrically borne by the property owner and the licensor, generally to the detriment of the latter[339], thus leading to theoretical doubts on equating a commons situation with an anticommons.

Behavioral economic studies have further brought the initial formalistic assumption into question. A 2006 study by Vanneste et al. showed that in different variants of commons/anticommons scenarios, subjects 1) consistently demanded higher payments for usage rights in an anticommons setting than what they themselves used in a commons, and 2) anticommons lead to a greater level of underuse than commons to overuse.[340] If generalized, this leads to the conclusion that an anticommons is even more socially detrimental than a commons dilemma in the same situation. This implies that prospect

[334] Shapiro 2001, p. 124.
[335] EPO ESAB Report 2015 I, *passim.*
[336] *N.B: De jure* this should be impossible due to prior art concerns. Then again, so is the existence of this form of upstream patent thicket in general.
[337] Holman 2006, p. 631–632.
[338] See *e.g.*: Buchanan & Yoon 2000, p. 12.
[339] Parisi *et al.* 2005, p. 25.
[340] Vanneste *et al.* 2006, p. 116-117.

theorists overstate the importance of appropriation as a means to ensure the efficient production of innovative products, at least when it comes to complex technologies. Furthermore, in his considerably extensive and thorough study of the arguments of prospect theorists and anticommons theorists in relation to biomedical upstream patenting, Wang conclusively shows that prospect theory provides excessively high incentives to patentees, without taking to account the anti-competitive effects engendered by patents.[341] This leads Wang to conclude that prospect theory is an invalid model for ensuring optimal levels of innovation in the biotechnological industry.[342] Therefore it is possible to conclude that an anticommons situation should be avoided even at the risk of creating a commons problem.

4.4.1. Empirical studies on the existence of anticommons and patent thickets

Although it can be established that the biotechnological industry in general and synthetic biology by extension has the definite *theoretical* potential to develop anticommons and patent thickets, it is necessary to determine whether this has taken place in reality. In the case of established industries such as biotechnology, multiple patent landscape analyses and questionnaire studies have been conducted on the matter. Unfortunately, the same cannot be said for synthetic biology. No empirical studies dealing exclusively with the two problems as they relate to synthetic biology were discovered when researching this thesis. Given that the technology is still in its infancy, it is likely that such studies would not even produce meaningful results. The analysis must consequently be constructed through analogy by overviewing the empirical research on the existence of anticommons and patent thickets in the conceptual precursor industries of synthetic biology, namely biotechnology, the semiconductor industry, and computer technology. Such an analogy makes it possible to determine whether anticommons and patent tickets generally form easily in technologies which are often regarded as being inherently complex.

An oft-cited study in the prevalence of anticommons and patent thickets in the biotechnological industry is the 2003 US study by Walsh *et al.* regarding patents and licenses on biotechnological research tools. In conducting the study, they interviewed a total of 70 people that included industrial R&D executives, trade association personnel, university researchers, patent lawyers, and government officials.[343] The purpose of the interviews was

[341] Wang 2008, p. 264–288. *N.B.:* The exact arguments examined and conclusions reached in this study are far too numerous and voluminous to describe in this thesis. It is highly recommended that the reader review the study themselves.
[342] *Idem.* p. 288.
[343] Walsh *et al.* 2003, p. 292

to gain an insider perspective on whether patent proliferation had in fact resulted in fragmentation and overlap.[344] Regarding the transaction costs implied by fragmentation, a majority of representatives within the industry stated that the large number of patents was less of a problem than it seemed, as the hundreds of potentially pertinent patents could be whittled down to only a few that required licensing.[345] Royalty stacking was not considered a major concern.[346] In general, the study found that only a relative few research project was abandoned due to anticommons or patent thicket considerations.[347]

A patent landscape analysis of European and US patents by Huys *et al.* relating to genetic diagnostic testing showed that while 25% of the patents studies were on genetic sequences, only 3% of patents in the entire study could be considered blocking patents[348], which implies the non-existence of an anticommons or patent thicket in genetic patenting. Possibly the most revealing study in this category is a 2015 patent analysis of global scope by Liddicoat et al. focusing on gene diagnostic tests with blocking patents. They find that such blocking patents may play a role in the United States and Japan, but the situation in Europe is considerably less marred by such concerns.[349] In analyzing the results of these studies and other similar ones, van Overwalle even goes as far as to claim that the notion of anticommons and patent thickets should finally be put to rest in the issue of genetics patenting.[350]

Does this mean that anticommons and patent thickets are a non-issue and prospect theory is empirically vindicated after all? Studies conducted by *inter alia* the EPO indicate otherwise. As an example, a 2013 EPO report by the Economic and Scientific Advisory Board identifies several problematic manifestations of patent thickets in relation to European patents, with multiple industries based on complex technologies exhibiting high levels of pendency, decreasing quality of applications, lack of transparency in ownership, increasing search costs of determining prior art, and an increased willingness of patent holders to litigate.[351] Regardless, the empiric studies discussed in the previous paragraphs would strongly suggest that the biotechnological industry is in no immediate risk of forming either anticommons or patent thickets. Is it likely to be a non-issue in synthetic biology as well? Assuming that it

[344] *Idem*. p. 292–293.
[345] *Idem.*
[346] *Idem.* p. 300.
[347] *Idem.*
[348] Huys *et al.* 2009, p. 908.
[349] Liddicoat *et al.* 2015, 349–351
[350] van Overwalle 2016, p. 29.
[351] EPO ESAB Report 2013, p. 9–11.

will not be of relevance disregards the fact that SynBio combines approaches from multiple fields of technology, such as the aforementioned semiconductor industry and computer technology industry. Empiric studies discussing the prevalence of the two problems as they relate to these industries paint a very different picture than what might be inferred from biotechnology alone.

An illuminating study in this respect is the 2013 study conducted by the UK Intellectual Propety Office (UKIPO) on the existence of patent thickets within various industries that have been granted European patents.[352] The specific form of patent thicket discussed in the study is a *triple*. Developed by von Graeveniz et al., a triple is a conceptual form of a minimal patent thicket in which three companies each possess blocking patents to the applications of the other two.[353] As for the existence of such triples in European patents granted by the EPO, the UKIPO confirmed that the biotechnology industry exhibits low levels of triple-type patent thickets, with only 0.9 triples per 1000 patents out of a study-wide average of 38.6 triples per 1000 patents. However, the situation is markedly different both in the semiconductor industry (105.5 triples/1000 patents) and the computer technology industry (95.5 triples/1000 patents).[354]

The general case presented by the empirical studies discussed in this section would indicate that complex technologies exhibit constantly increasing levels of patenting, but the actual formation of anticommons and/or patent thickets is not a given.[355] While the situation in the biotechnological industry is encouraging in this respect, the results of the UKIPO study regarding the other precursor industries of synthetic biology are considerably less so. If the SynBio practitioners that follow the IP frame adopt patenting practices that are similar to the semiconductor and computer technology industries, the end result might very well resemble the anticommons and thickets found in those industries, along with the full spectrum of concomitant economic inefficiencies they entail.

4.4.2. SynBio anticommons and patent thickets

The attention now turns to assessing the aforementioned likelihood of an IP frame in SynBio resulting in an anticommons and/or patent thicket. As indicated above, most of the literature involves the more general case of the potential for anticommons and patent thickets in

[352] UKIPO Patent Thicket Study 2013
[353] von Graevenitz *et al.* 2011 p. 7.
[354] UKIPO Patent Thicket Study 2013, p. 53.
[355] See e.g. *idem.* p. 43–46.

biotechnology, with relatively few studies devoted exclusively to its applicability to synthetic biology in particular.[356] Following the approach adopted in the previous empiric section, this assessment is constructed through analogies to the predecessor technologies of synthetic biology.

First and foremost, it must be reiterated that synthetic biology is a cumulative technology, meaning that it requires multiple vertically structured enabling technologies to produce downstream applications.[357] Colangelo argues that industries that feature such cumulative innovation are highly prone to develop IPR anticommons and patent thickets.[358] One might very well argue that since biotechnology has not exhibited these effects, they are likely not to be of consequence in SynBio. This argument would disregard certain important factors. As stated in section 2.1. of this thesis, it is the modularity of SynBio constructs which differentiates it from pre-existing forms of biotechnology. If its potential becomes reality, the iterative assembly of bioparts into devices, devices into systems, and systems implemented in a chassis is more similar to constructing a computer from components than it is editing a gene.

As an outgrowth of biotechnology, synthetic biology contains all the cumulative aspects of the former while making considerable additions to it. The result of this is that synthetic biology entails considerably higher levels of cumulative innovation than other forms of biotechnology. A developed form of SynBio may indeed likely resemble e.g. the semiconductor industry more than it does traditional biotechnology. Wellhausen and Oye state that this is partially due to the fact that, compared to historically preceding subfields of biotechnology, synthetic biology simply has more material that may fall within the scope of IPR protection. In addition to the aforementioned modular standardized parts, IPR protection can be extended to assembly and performance standards, device and system design, and the research tools to create and combine all of the above.[359] The situation could be even worse: Montague et al. have opined that any practical application of synthetic biology will necessarily go beyond the strict confines of pre-existing metabolic pathways, with efficient systems requiring dozens of additional modifications to different parts of the genome.[360] Such changes to other parts of the genome carry the risk of infringing patents that are *prima*

[356] *N.B.:* Multiple studies to however discuss the possibility, such as Henkel & Lüttke 2014, p. 16; and de Miguel Beriain 2014, p. 204–206.
[357] Agovic 2014, p. 105.
[358] Colangelo 2004, p. 21.
[359] Wellhausen & Oye 2008, p. 2.
[360] Montague *et al.* 2012, p. 659.

facie unrelated to the system under development. Following a generally similar line of argumentation leads de Miguel Beriain to conclude that due to the varied nature of upstream patents required in synthetic biology, at least some of which are likely to be blocking, coupled with the varying incentive structures of the actors in the field, the formation of an anticommons seems quite likely.[361]

Therefore it can be concluded that there exists a definite possibility that the IP frame of synthetic biology may result in a fragmented and overlapping patent landscape. While not by any means a definitive and conclusive argument, given the welfare-reducing effects of anticommons and patent thickets both on downstream innovators and, through a decrease of dynamic efficiency, society at large, I would argue that it is better to err on the side of caution. If one is to accept the notions put forth in section 1.2. of this thesis regarding the necessity of an *ex ante* framework for the managing of emerging technologies, some pre-emptive measures are worth considering. However, given the as-yet hypothetical nature of the risk of fragmentation and overlap in synthetic biology, this cautionary approach should not result in drastic measures that would only be warranted by a total collapse of all potential innovation within the field. It merely emphasizes the importance of one of the initial conditions set for any normative solutions that this thesis may contain: simplicity.

[361] de Miguel Beriain, 2014, p. 204–205.

5. The normative logic of solving fragmentation and overlap

5.1. Normative standard

Constructing a normative approach to the problems outlined above requires some standard of measurement for the patent system. One obvious line of reasoning for constructing such a measurement is to return to the fundamental ideas described by Machlup and Penrose. Their third argument is the most pertinent in this case, i.e. creating an incentive to innovate. Moreover, neither prospect theorists nor anticommons theorists have disputed the role of patents as a means of engendering innovation; they merely seek to optimize this logic.

As discussed previously, one fundamental elements of both this thesis and the patent system in general is the primacy of optimal dynamic efficiency in generating welfare. Following Colangelo's approach, this mode of though provides us with the necessary standard of measurement for the efficiency of the patent system: maximizing the difference of value between the static inefficiency of social losses incurred by the creation of exclusionary rights and that of the dynamic efficiency resulting from new innovations such exclusionary rights have made possible.[362] As a corollary to this logic, if the patent system results in the creation of exclusionary rights while also stifling innovation, a patent monopoly is unjustified. Given the conclusions of the previous chapter, it seems evident that the formation of an anticommons and/or patent thicket in the field of synthetic biology is the most pressing concern in this respect. The remainder of this thesis is devoted to discussing measures that may reduce the risks posed by a potentially fragmented and overlapping patent landscape.

5.2. Network effects as a source of efficiency

Henkel and Maurer have delineated three important economic characteristics of a functional parts-based synthetic biology paradigm: 1) the (bio)parts that compose devices will be reused, 2) each *de novo* assembly of such parts will be a costly endeavor, 3) reusing parts in new devices reduces costs, provided that the new experiment is constructed using a similar metabolic pathway as the preceding ones.[363] Following this line of argumentation leads them to conclude that a parts-based approach in synthetic biology exhibits positive consumption externalities, more commonly known as *network effects*.[364] In practical terms this means that

[362] Colangelo 2004, p. 18.
[363] Henkel & Maurer 2007, p. 1
[364] *Idem.* p. 2

the general willingness to use a biopart increases the more others have used it[365], as the marginal costs across the entire network are lowered by subsequent use. As shown by Katz and Shapiro, network effects are a common occurrence in markets with complementary goods.[366] Therefore it is hardly surprising that such an effect shows up in synthetic biology, as the bioparts approach is fundamentally based on combining complementary parts to construct devices and systems.

Network effects can create sufficiently high positive externalities to mitigate some of the harmful effects arising in patent monopolies. One classical example of monopoly behavior is that a monopolist is incentivized to limit supply through a decrease in the production of the monopoly good so that marginal cost equals marginal revenue, which results in the maximization of the monopolist's payoff.[367] When discussing intellectual property, the analogous behavior is to limit access to a proprietary technology by means of the exclusionary property of patents, allowing the patentee to charge monopoly-type royalty payments for licenses.[368] If this results in monopoly royalties being sufficiently high, it would imply the stifling of network effects, as the use of upstream proprietary IPRs remains low due to high royalty fees.[369] However, if the potential network externalities are high enough, the patentee monopolist benefits more from the expansion of the network than from charging monopoly prices for licenses to their patents in a single instance.[370] In practical terms, this means that all the patentees within a technological field might be strategically inclined to make licenses to their technologies as easy to obtain as possible, in hopes of benefitting from network externalities resulting from the adoption of their technologies.[371] The logical result of this is that in the presence of sufficiently high network effects, the patentees would seek to coordinate their efforts to reduce royalty stacking, hold-up, and transaction costs. One practical way of doing this is through offering licenses to downstream developers for a fair price[372], or even royalty free[373].

The network benefits may extend to the licensing agreements themselves. In this vein, Korobkin has noted that the standardization of contract terms can lead to their own network

[365] Economides 1995, p. 212.
[366] Katz & Shapiro 1994, *passim.*
[367] Cooter & Ulen 2004, p. 36.
[368] *Idem.* 122–123.
[369] Buchanan & Yoon 2000 p. 9–10.
[370] Economides 1995, p. 213.
[371] *Idem.*
[372] See *e.g.*: Sidak 2013 *passim* for a full explanation of the economic logic of this model.
[373] See *e.g.*: Van Overwalle 2016, p. 21–22.

benefits, as they are more likely to face adjudication early on, leading to a greater shared understanding of the specifics and implications of the terms. Standardized terms also naturally reduce the aforementioned bargaining costs through lowering contract negotiation and drafting costs.[374] The combination of both technological and contractual network effects has led to the creation of standard licenses in many of the precursors of SynBio, such as by in the electronics industry.[375] As for ensuring similar effects in synthetic biology, one practical way in which both forms of network effects may be attained is through a SynBio parts-monopolist encouraging the use of its proprietary bioparts by licensing its IPRs on standardized fair, reasonable, and non-discriminatory (FRAND) terms.[376]

The crux of the matter seems relatively straightforward then: network effects have the potential to mitigate royalty stacking, patent hold-up, and transaction costs in a developed form of synthetic biology, provided that the technology produces sufficiently high positive network externalities. Creating a system which encourages the emergence of such network effects is a valid way of ensuring the viability of the technology, which in turn has the potential to improve societal welfare. If such systems are not in place, it is a definite possibility that the positive network externalities fall short of the limit that encourages upstream patentees to cooperate both with each other and the downstream developers, which may result in a SynBio market that exhibits detrimental monopoly effects, such as royalty stacking, hold-up and suboptimal transaction costs, resulting in a welfare-suboptimal scenario.[377] This statement is also a specific case of the generalized normative logic of the patent system as presented in the preceding section.

5.3. Collective action problems

Network effects by themselves may be sufficient in mitigating some of the aforementioned problems related to the emergence of biopart-monopolists. However, they do not seem capable of addressing the fundamental forces that drive the creation of fragmentation and overlap. Synthetic biology research is conducted all around the world, resulting in the more likely scenario of multiple patent holders.[378] As such, the transaction costs described in section 4.3.1. of this thesis apply equally to patentees that seek to coordinate their efforts. As an extension of that logic: the more patentees there are, the more difficult it is to for them

[374] Korobkin 2000, p. 128.
[375] Chappatte 2009, p. 322.
[376] Contreras *et al.* 2015, p. 24–25.
[377] Henkel & Maurer 2007, p. 2.
[378] Oldham et al. 2012, p. 5.

to generate network externalities as the costs of coordination increase. This raises an important point: solving the fundamental problems of fragmentation and overlap are a *prerequisite* for the creation of positive network externalities. A logical follow-up question in this line of reasoning is: can such network effect-generating solutions be constructed by free market actors without institutional intervention?

Let us assume that Henkel and Maurer are correct in stating that SynBio inventions will exhibit network effects. In the case of overlap, it crucial to highlight the fact that while its effects may be mitigated by patentee coordination, it is fundamentally an *institutional problem* arising from faults in the patenting process itself.[379] In the case of fragmentation, which is effectively a problem generated by the patentees themselves[380], a network solution may be possible. However, one might naïvely assume that since cooperation is required for generating network effects, which are beneficial to both the patentees as a group and society at large, synthetic biology innovators and IPR holders will automatically choose to cooperate. Such an assumption would disregard the potential for *collective action problems*.

In his influential book *The Logic of Collective Action,* Mancur Olson noted that the best collective outcome requires that it is also in the interest of all of the private individuals involved in bringing about that outcome to perform the functions required of them.[381] If the individuals in a group must make sacrifices or expend resources to attain a common goal, an individual may be tempted to benefit from the outcome without commensurate participation the effort to bring it about, unless the participation itself is beneficial to the individual.[382] A rational individual will evaluate the strategies of cooperation and non-cooperation (henceforth referred to as *defection*) and choose the strategy that results in the most beneficial outcome to themselves. As all the rational individuals involved in the collective action do the same thing, the result is a confluence of strategic behavior, requiring every individual to evaluate the strategies of other individuals in order to discover the optimal course of action.[383] Ensuring proper collective action in such an environment requires providing selective and separate incentives to the individual decision makers, thus aligning the goals of the group and the individuals that comprise it.[384] Attaining this goal requires a more

[379] van Overwalle 2016, p. 6.
[380] *Idem.*
[381] Olson 1971, p. 50.
[382] *Idem.*
[383] Cooter & Ulen 2004, p. 38.
[384] Olson 1971, p. 51.

detailed understanding of the strategic behavior of the individuals of the group, which can be accomplished by the tools provided by game theory.

As the previously exposited logic of collective action problems indicates, joint-action agreements are not enforceable, i.e. the game is *non-cooperative.*[385] The symmetry of the decision making process allows the players to know the strategic options of their opponents, meaning that the game is one of *perfect information.*[386] The purpose of each player is to maximize their individual *payoff*[387] by choosing the best response to the strategic decisions of other players[388]. In collective action games, the social optimum is the solution that maximizes the total payoff of the players.[389] The situation presented above has the same incentive structure as the famous *Prisoner's Dilemma*, in which two players are similarly given a choice between two strategies: cooperate or defect. The variables in the following payoff table can be replaced with any numeric values, provided that the replacement values conform to the following relationships: $T > R > P > S$ and $R > (S + T)/2$. The structure of the payoff table is the following[390]:

Figure 2.
Payoff table

		Y	
		Cooperate	Defect
X	Cooperate	R, R	S, T
	Defect	T, S	P, P

The objective is to determine the *Nash equilibrium*, i.e. which strategy offers the players the best possible payoff while taking into account the best strategy of the other player.[391] If player X assumes that Y will cooperate, the optimal strategy for X is to defect, because $T > R$. If player X assumes that Y will defect, the optimal strategy for is to defect as well, because $P > S$. Regardless of what Y chooses, defecting is X's *dominant strategy*.[392] Because the situation is symmetrical, the same holds true for Y. The result of the collision of these dominant strategies is the Nash equilibrium: [P, P]. The nature of this dilemma results from the fact that by cooperating, both would receive payoff [T, T], which is more socially optimal

[385] Dixit *et al.* 2009, p. 26.
[386] Motta 2004, p. 542.
[387] Dixit *et al.* 2009, p. 28–29.
[388] Motta 2004. p. 543.
[389] Dixit *et al.* 2009, p. 449.
[390] Axelrod & Hamilton 1981, p. 1392. *N.B.:* In this format of payoff tables, the first value is the payoff X receives and the second is that of Y. If written out, [T, S] means "X will receive T, Y will receive S".
[391] Cooter & Ulen 2004, p. 41.
[392] Dixit *et al.* 2009, p. 98.

than the Nash equilibrium, as T > P.[393] In terms of classical economics, the rational pursuit of their self-interest results in both players receiving a Pareto inferior payoff.[394] Following Thomas Schelling's methodology, this logic can be extended to an *N*-person group[395], which results in a strategic explanation of this form of collective action problem.

One way to search for solutions is to recognize that the situation described above is only a single instance of decision making, whereas in real life, such one-off transactional relationships are relatively rare. If players engage in an ongoing relationship, such as a contractual arrangement, it effectively results in multiple iterations of the game with no predetermined end point, turning it to a *continuously iterated prisoner's dilemma,* in which the Nash equilibrium may contain the option of cooperation.[396] The so-called *folk theorem* indicates that all of the aforementioned contingent strategies are viable given certain values in the payoff table.[397] This means that the players must take into account previous and future iterations of the game when making the decision to cooperate or defect in every subgame. Strategic behavior in such a scenario is determined by so-called *contingent strategies*, meaning that the players have a pre-defined notion of how respond to the actions of other players in future games.[398] In continuously iterated games, players have three classical contingent strategies available: 1) *limited period of punishment* for defection, in which a player punishes another for defecting for a pre-determined amount of future iterations, 2) *grim trigger,* in which a player cooperates until the second player defects, after which the first player punishes the second player by choosing 'defect' in all future games, and 3) *tit-for-tat (TFT)*, in which a player always chooses the same strategy as the second player chose in the preceding instance of the game.[399] The theoretical solution to such a configuration requires that one determines the *subgame perfect Nash equilibrium*, which is wholly dependent on the discounted values of the payoffs in future iterations of the game. However, one does not need to rely purely on theory in solving the matter, as Axelrod and Hamilton famously showed that in simulated games of millions of iterations, TFT is the optimal contingent strategy in terms of highest total payoff produced.[400]

[393] Axelrod & Hamilton 1981, p. 1392
[394] Viscusi *et al.* 2005, p. 773.
[395] Schelling 2006, p. 217–243.
[396] Le & Boyd 2007, *passim.*
[397] See *e.g.*: Ely & Välimäki 2002, p. 84–88.
[398] Dixit *et al.* 2009, p. 401
[399] *Idem.*
[400] Axelrod & Hamilton 1981, *passim,* coming to the conclusion above on p. 1394.

The third and final means of ensuring the socially optimal outcome is to alter the payoff matrix and its underlying incentive structure.[401] Given that the underlying issue here has to do with aligning intellectual property rights, which are legal institutions, this would imply a change to those institutions through legislative or regulatory intervention.[402] Furthermore, this approach can be combined with the second solution, resulting in a clear normative logic for solving the problem of collective action: institutional intervention that ensures the market actors are likely adopt a TFT strategy in their ongoing relationship. The legal implication of this idea is to remove all unnecessary hindrances in allowing patentee cooperation.

5.4. Non-aligning incentives

As shown above, resolving the collective action problem through adopting a model of cooperation is generally in the interests of the SynBio patent holders and licensors themselves, as they themselves will find it just as difficult to navigate the anticommons and patent thicket as any new downstream developer. De Miguel Beriain has noted that this has an extended effect on investors in such proprietary research endeavors, as a great deal of their investment into synthetic biology R&D might be spent on licensing fees, thus reducing the likelihood of valuable innovations and their commensurate return on investment.[403] A similar empirical point is put forth by Ramirez, who states that proprietary research tools have been adopted by researchers despite private ownership[404], and that research communities have a consistent vested interest in sharing scientific materials[405]. Building on this argumentation, one could easily come to the conclusion that since the best way for solving the collective action problem and generate network effects is for the IP holders actors in the field is to adopt a tit-for-tat contingent strategy, no other measures are needed. If truly rational, the IP market actors can address fragmentation issues themselves.

While it can be concluded that the proposition given above is generally true for actors that have a vested interest in either conducting their own research or generating network effects, this view does not take into account so-called *Patent Assertion Entities* (PAEs), more commonly known as "patent trolls".[406] PAEs are companies whose objective is to attain a patent portfolios that enables them to seek rents through licensing fees or damages through

[401] Viscusi *et al.* 2005, p. 774.
[402] *Idem.* p. 774–775.
[403] de Miguel Beriain 2014, p. 205.
[404] Ramirez 2004, p. 374–378.
[405] *Idem.* p. 378–384.
[406] *N.B.:* the literature abounds in various other terms for these entities, such as 'non-producing entities' (NPEs) and 'patent sharks'.

patent infringement litigation.[407] Harris convincingly argues that as their main rationale is to acquire blocking patents that they can subsequently use to extract as high royalties as possible, PAEs do not generally seek to further the technological field itself and are thus strategically indifferent when it comes to the dynamic inefficiencies generated by innovation.[408] Furthermore, PAEs generally *benefit* from both fragmentation and overlap.[409] It is theoretically possible that PAEs would also seek network benefits by expanding the technology, but only for the purposes of attracting new downstream developers from which to extract rents.

The take-away message from this discussion is that not all potential actors in a future SynBio IP frame may necessarily share the same incentive structure. For example, if a PAE manages to acquire a SynBio standard-essential patent in order to extract maximal rent from it, it is likely to affect collaboration between the producing patentees as well as limit possible network externalities. In terms of game theory, if one person defects, it is likely that others will defect as well. This implies that solving both fragmentation and overlap requires multiple solutions, depending on what type of entity those solutions address. If the SynBio patent landscape fragments, one set of solutions involves the upstream *producing entities*[410] involved in synthetic biology collaborating to form coherent property structures that they can subsequently license. The second set of solutions requires that measures to limit the effects generated by actors that have an incentive to produce welfare-detrimental effects, such as the aforementioned PAEs. A discussion on these tools forms the basis of the next chapter.

[407] Gerardin 2016, p. 2.
[408] Harris 2014, p. 297–300.
[409] *Idem.* p. 285–290.
[410] Shapiro 2001, p. 127

6. Approaches for constructing a viable SynBio framework

6.1. Market cooperation for reducing fragmentation in SynBio

A great deal of scholarly interest has been devoted to studying various free market models of patent management that may potentially solve fragmentation, as well as ameliorate overlap, in complex technologies. Van Overwalle et al. identify three free market approaches commonly raised as means of overcoming the negative effects of fragmentation in the life sciences: cross-licensing, patent pools, and patent clearinghouses.[411] While broad agreement exists that these instruments have the potential to assist in the development of synthetic biology as well[412], not a great deal of actual literature seems to exist in relating these generalized models to synthetic biology, although generalized statements of their possible utility in the life sciences are abundant.[413] In their recommendations, Minssen et al. emphasize the importance of further study on their applicability to synthetic biology[414], which is the primary purpose of this section. The following approach is constructed in a similar way as in chapter 4.4. of this thesis, namely through analogies to how such tools are used in the management of IPRs in general and how they might be adapted to fit the uses of the IP frame in synthetic biology.

6.1.1. Cross-licensing

One commonly suggested general solution to patent thickets in particular is *cross-licensing,* which is a free-market arrangement that entails the reciprocal removal of the effects generated by blocking patents.[415] The general situation in which such a solution is applicable is if two patentees have complementary patents that block both from developing a new invention. A cross-licensing occurs when the patentees reciprocally allow each the use of their blocking technologies, thus untangling any patent thicket that may hinder innovation.[416] Commentators such as Shapiro have extolled the virtues of cross-licensing as a means to reduce the harmful effects of patent thickets by making bilateral licensing unnecessary in a blocking situation.[417]

[411] Van Overwalle *et al.* 2006, *passim.*
[412] See e.g.: Minssen *et al.* 2015, p. 238; OECD SynBio Report 2014, p. 12.
[413] See e.g.: van Zimmeren et al. 2011, *passim.*
[414] Minssen *et al.* 2015, p. 208, Recommendation 5.
[415] Motta 2004, p. 206.
[416] Shapiro 2001, p. 127.
[417] *Idem, passim.*

Cross-licensing as a method to deal with potential SynBio has its limits. Although cross-licensing requires simpler arrangements than pure bilateral licensing, it still is inherently bilateral. Cross-licensing implies the negotiation of a series of agreements between varying upstream patentees, resulting in a tangled web of contractual arrangements that is complicated to manage.[418] In second, it also requires that each new upstream innovator engages in a series of such bilateral negotiations, thus not resolving the issue of transaction costs inherent in fragmentation and overlap. However, it would be incorrect to state that cross-licensing has no effect on such costs. Shapiro has highlighted the fact that any successful cross-licensing arrangement will reduce the bargaining costs *viz.* a normal licensing situation.[419] In third, cross-licenses are only useful in the same level of cumulative innovation, as a new downstream developer might not have any patents to cross-license.[420] Given the cumulative nature of synthetic biology as discussed in section 4.4.2., it is likely that many downstream developers of synthetic biology will not benefit from cross-licensing.

Furthermore, real life arrangements have a tendency not to be purely bilateral. As an example, the triple thicket model developed and studied by von Graevenitz et al. has a configuration in which bilateral cross-licensing is insufficient means to resolve blocking patents: even if two parties conclude such an arrangement, the third party in the triple may still block any applications developed by the cross-licensing parties.[421] Given the prevalence of patent triples in certain precursor industries of synthetic biology[422], emphasizing cross-licensing as a solution is unlikely to result in significant progress. Compounding this issue is the fact that the triple thicket is a *simplistic representation* of patent thickets. Instead of a trilateral blocking situation, any number of patentees might find themselves in a reciprocal blocking situation, requiring an N-lateral cross-license in order for the thicket to be resolved.

Based on the argumentation above, it can be concluded that cross-licensing alone is insufficient as a means for the free market to solve the potential issues of fragmentation and overlap arising in synthetic biology. It might be a useful tool in resolving certain simple blocking situations in the technological upstream, but insufficient as a remedy for the underlying problems.

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[418] *N.B.:* Shapiro 2001, p. 130 discusses the existence of such cross-licensing webs, but concludes that their advantages are empirically verifiable. This notion can be accepted while emphasizing the fact that they nevertheless are not the *ideal* solution.
[419] *Idem.* p. 129–130.
[420] van Zimmeren et al. 2011, p. 570.
[421] von Graevenitz et al. 2011, p. 9.
[422] See e.g.: von Graevenitz *et al.* 2011, p. 10, Table 1; UKIPO Patent Thicket Study 2013, p. 53.

6.1.2. Patent pools

A more refined solution is to adopt a collaborative licensing model that effectively aggregates patent rights into a *patent pool.*[423] Patent pools are similar to cross-licensing in that they consist of two or more patent holders granting each other licenses to one or more of their patents.[424] The difference to cross-licensing arises from the fact that it is not an *ad hoc* solution between two patentees. The patents are pooled in a way which allows them to be licensed to third parties as a complete package.[425] Depending on the structural arrangement desired by the founders of the pool, licenses to the entire bundle of patents may be granted either directly by the patentees or indirectly, in which case it is usual for an institutionally separate entity to manage both the patent pool and the granting of licenses to the pooled technologies.[426] Patent pools have been created in the life sciences, although with variable success. One such example is the BIO Ventures for Global Health pool for patents relating to neglected tropical diseases.[427]

It is generally accepted that patent pools improve welfare only if they contain complementary patents.[428] If a patent pool fulfils that requirement, they are a considerably more effective way of addressing potential patent fragmentation in SynBio than cross-licensing. Instead of having to negotiate a multitude of license agreements for e.g. proprietarty bioparts, a downstream innovator could obtain the necessary rights from a "one-stop shop"[429], consequently reducing the potential for royalty stacking and hold-up.[430] Additionally, downstream innovators would not need to expend an inordinate amount of time tracking down both the relevant patents and their owners, thus reducing search costs. A single license to a bundle of upstream patents also naturally reduces bargaining costs.[431]

However, it would be naïve to conclude that a synthetic biology patent pool would constitute a panacea to fragmentation and overlap, transaction costs, and collective action problems. Instead of resolving these issues once and for all, the creation of such a pool might merely push the strategic and structural issues one step back. In first, a patent pools typically contain

[423] van Zimmeren *et al*. 2011, p. 570.
[424] Shapiro 2001, p. 127–128.
[425] Lerner *et al.* 2007, p. 610.
[426] Aoki & Schiff 2008, p. 195.
[427] Bio Ventures for Global Health Website
[428] Lerner & Tirole 2004, p. 691.
[429] Dequiedt & Versaevel 2013, p. 59.
[430] See e.g.: Lemley & Shapiro 2007, p. 2014–2015 for an explanation of the general case.
[431] WIPO Patent Pool Analysis 2014, p. 9.

patents in the same level of cumulative innovation[432], meaning that they primarily address issues of horizontal fragmentation. Parisi et al. have shown that strategies and tools for managing horizontal fragmentation do not necessarily resolve vertical fragmentation.[433] This implies that in fields of cumulative innovation, such as synthetic biology, multiple patent pools would need to be established for different levels of technological development, such as for enabling technologies, standards, biopart libraries, *et cetera.* The issue of collective action is not necessarily resolved by patent pools either. Participation in a patent pool entails opportunity costs, as a participant must effectively relinquish control of some of their patents, reducing their potential to extract holdup-type rents.[434] Following the logic of the game theoretical presentation in chapter 5.3., the participants have the exact same strategic incentives to maximize any benefits arising from the pool while minimizing their costs. This can potentially lead to three distinct collective action problems.

The first problem is that a participant in a patent pool agreement has the incentive of adding the absolute minimal amount of valuable patents to the pool, all the while hoping to benefit from the contributions of other participants and the possible network effects it might generate.[435] If the situation is symmetric for all participants, the result may be a pool that contains little to no valuable patents, essentially resulting in a "market for lemons" as defined by Akelof.[436] This has been a concern with existing patent pools in the life sciences.[437]

In second, strategic behavior in the period preceding and coinciding both with cross-licensing or the creation of a patent pool may also exacerbate fragmentation and overlap. As an example, one way for a patentee to provide sufficient material to warrant the cross-license inherent in both arrangements is to engage in *portfolio aggregation*.[438] This implies a situation in which a patentee, instead of applying for a single patent containing multiple innovative technologies, seeks as many individual patents for their innovations as possible in order to inflate their patent portfolios and consequently improve their bargaining position.[439] This may worsen the lemons market problem discussed above, while resulting in no appreciable change in the underlying problem of patent fragmentation.

[432] Aoki & Schiff 2008, p. 195.
[433] Parisi *et al.* 2005, p. 21–25.
[434] Aoki & Schiff 2008, p. 201.
[435] Choi 2010, *passim.*
[436] Akerlof 1970, *passim.*
[437] Van Overwalle 2016, p. 26–27.
[438] Wagner & Parchomovsky 2005, p. 35–36.
[439] *Idem.*

The third problem has to do with the formation of the pool itself. Even if the issues discussed above were resolved, it might be strategically optimal for a patentee not to participate in the pool at all.[440] If the prospect of pooled patents offered at reasonable royalty rates generates sufficient interest in downstream developers to engage in a project that requires the pooled patents as inputs, a patentee possessing a blocking patent that has not been included in the pool would be able to demand extortionate royalties for the last missing piece of the upstream patent puzzle.[441] Continuing with the assumption that the situation is symmetric for all potential participants of the pool results in no pooling of patents. The intractable nature of these three collective action problems indicates that pools are a valuable tool, but in order for them to function, (supra)governmental actors should consider intervening in the market to force optimal collective action, namely to impose the TFT contingent strategy. The methods of doing so will be discussed in section 6.2.2.

6.1.3. Patent clearinghouses

Another way of approaching the issue is to create a *patent clearinghouse* for synthetic biology. Patent clearinghouses are institutions which seek to match patentees with licensees in an effective manner[442], broadly similar to how clearinghouses act as an intermediary between buyers and sellers in the financial industry. This model has distinct benefits in relation to synthetic biology. First, Aoki and Schiff have shown that clearinghouses often generate all-important network effects.[443] Second, Falce has noted that clearinghouses have a special capacity in attracting SMEs, resulting in the formation of a system that is akin to a commons.[444] Given the relevance of the commons approach in synthetic biology, a clearinghouse for the IP frame could be beneficial, as it would mirror the general approach of the A2K model, thus raising the possibility of increased compatibility between the two.

In her study on the forms of clearinghouses prevalent in the life sciences industry in general, van Overwalle distinguishes between four functionally different types of clearinghouses: information clearinghouses, technology exchange clearinghouses, standardized license clearinghouses, and royalty collection clearinghouses. Each of these models have different economic implications in managing the costs generated by fragmentation and overlap.

[440] Aoki & Schiff 2008, p. 201.
[441] *Idem.*
[442] Van Overwalle 2016, p. 12.
[443] Aoki & Schiff 2008, p. 200.
[444] Falce 2011, p. 51–52.

Information clearinghouses are the simplest of the aforementioned systems. They seek to provide a platform for the sharing and exchange of technical knowledge or information relating to the proprietary status of that knowledge.[445] This definition includes all registries operated by patent authorities. This type of clearinghouse has the benefit of reducing the search costs engendered by fragmentation by providing downstream patentees with a means to seek out the relevant patents.

Technology exchange clearinghouses provide a platform for patentees to essentially advertise their patents to potential licensees. A technology exchange clearinghouse collects a listing of such technologies, enabling downstream developers to consult a single resource on what technologies and patents might be relevant, as well as the contact information of the licensor of that technology.[446] In addition, a technology exchange may provide some additional facilities that engender cooperation, such as providing model licensing agreements for parties to utilize.[447]A prominent example of a technology exchange clearinghouse in the life sciences is the WIPO Re:Search platform.[448] This type of clearinghouse may reduce transaction costs to a greater extent than an information clearinghouse by further reducing search costs, as well as possibly limiting some of the duplication of licensing arrangements.

Standardized license clearinghouses builds upon technology exchange clearinghouses by providing the opportunity to directly license the patented technologies listed in the clearinghouse.[449] The term 'standard' does not imply an identical license agreement for all instances, instead referring to a type of modular licensing agreement, containing a range of pre-prepared options that the licensors and licensees may use to construct a license.[450] Examples of such arrangements include Librassay, a standardized license clearinghouse operated by the private company MPEG LA, which offers access to patents involving tests relating to personalized medicine.[451] This system has the benefit of drastically reducing transaction costs by both reducing the search costs involved in locating relevant patents, as well as the bargaining costs by removing the need to negotiate separate licenses.

[445] Van Overwalle 2016, p. 13
[446] *Idem.*
[447] *Idem.*
[448] See: WIPO Re:Search website
[449] Van Overwalle 2016, p. 13.
[450] *Idem.* p. 13–14.
[451] See: Librassay website

One final form described by van Overwalle is the *royalty clearinghouse*, which combines the functions of all of the above, as well as manages the royalty fees involved in the licensing agreements. It is conceptually very similar to how performance rights organizations, such as the Finnish *Teosto*, operate in issues relating to copyright.[452] However, van Overwalle states that no such organizations currently exist within the life sciences.[453]

The most notable effect of the clearinghouse models is their capability to reduce transaction costs.[454] However, the models presented above generally leave the underlying patent landscape fragmented, resulting in their general inadequacy as solutions to potential royalty stacking in the synthetic biology downstream.[455] Compared to the first two models, a standardized license clearinghouse and royalty clearinghouse have the benefit of addressing patent hold up to some extent, as they effectively remove the possibility for strategic bargaining on part of the patentees. As a form of license marketplace, clearinghouses may also be capable of ameliorating the search costs that are specific to cumulative innovation by providing a coherent sources of information on enabling technologies, thus reducing some of the detrimental aspects of vertical fragmentation. Despite their promise, scholars have raised concerns regarding the viability of most clearinghouses in the life sciences (save for information clearinghouses), as the reduction in bargaining power leads to similar incentive problems as in patent pools, possibly resulting again in a "market for lemons".[456] As with patent pools, possible solutions to this problem will be discussed in section 6.2.2.

6.1.4. Competition policy in relation to the pooling of patents

Both scholars and legislators have noted that aligning the incentives of competing innovators through cross-licensing or patent pools has the potential to result in anti-competitive behavior.[457] In this vein, it is vital to note that TFEU Article 101(1) prohibits:

> *"[A]ll agreements between undertakings, decisions by associations of undertakings and concerted practices which may affect trade between Member States and which have as their object or effect the prevention, restriction or distortion of competition within the internal market, and in particular those which limit… (b)…technical development…"*

[452] Van Overwalle 2016, p. 14.
[453] *Idem.* p. 19.
[454] Aoki & Schiff 2008, p. 202.
[455] *Idem.*
[456] Van Zimmeren *et al.* 2011, p. 574.
[457] See e.g.: Shapiro 2001, p. 127, along with practically every single reference used in this chapter.

TFEU Article 101(3) delineates the scope of this prohibition by allowing agreements, decisions and concerted practices of undertakings which contribute to promoting technical and economic progress, while allowing consumers a fair share of the resulting benefit. Such agreements, decisions, and practices may not impose restrictions that are not indispensable or allow the undertaking to eliminate competition. The European Commission has clarified the exact relationship of the aforementioned norms by issuing the Block Exemption Regulation (EU) No. 316/2014 on Technology Transfer Agreements (TTBER)[458] and the communication on Guidelines on the Application of Article 101 of the TFEU to Technology Transfer Agreements (TTA Guidelines)[459]. As a general point, it must be noted that paragraph 247 of the TTA Guidelines specifically states that TTBER does not apply to 'technology pools', which is the phrase used in the document to denote patent pools.[460]

Paragraph 291 of the TTA Guidelines contains a safe harbor provision regarding the creation and operation of patent pools. It creates seven conditions for a patent pool which must be fulfilled in order for the pool to be fall beyond the scope of TFEU Article 101(3). These conditions are: 1) participation in the patent pool must be open to all interested parties, 2) safeguards that ensure the inclusion of only essential technologies into the pool must be placed, 3) safeguards that restrict the exchange of sensitive information that is not relevant for the operation or creation of the pool must be adopted, 4) licensing technologies into the pool happens non-exclusively, 5) licensing out of the pool follows fair, reasonable, and non-discriminatory (FRAND) terms, 6) the right of challenging the validity and essentiality of the technologies is not restricted, and 7) contributors and licensees to the pool are allowed to develop competing technologies.

Paragraphs 250–255 of the TTA Guidelines discuss the nature of the technologies included in patent pools and their potentially anti-competitive effects. Paragraph 255 provides that forming technology pools that contain mostly *substitute technologies* will generally be considered as a violation of TFEU Article 101(3), as coordinating the licensing of substitute technologies may easily amount to price fixing. In this respect, it also must be noted that point 2 of the safe harbor gives reason to pause, given that it specifically refers to *essential technologies.* The definitions contained in paragraphs 251 and 252 essentially equate these

[458] Commission Regulation (EU) No 316/2014 of 21 March 2014 on the application of Article 101(3) of the Treaty on the Functioning of the European Union to categories of technology transfer agreements (L93/17)
[459] Communication from the Commission: Guidelines on the application of Article 101 of the Treaty on the Functioning of the European Union to technology transfer agreements (2014/C 89/03)
[460] See: TTA Guidelines, para. 244.

terms, by defining both as technologies that are required or essential "to produce a particular product or carry out a particular process to which the pooled technologies relate".

This results in a crucial concern: while generally complementary, it is not altogether clear whether all patents on the elements of the bioparts approach are essential as meant in the Guidelines. As an example, it might be advantageous to pool IP relating to various forms of minimal genome chassis so that a downstream developer may test the efficacy of their biosystem implementation in multiple chassis. Different chassis exhibit codon bias, meaning that they have a tendency to favor certain codons over synonymous ones when encoding mRNA, which has implications for the functioning and design of biosystems.[461] Given that it is still possible to use a non-optimal chassis for a biosystem[462], are the chassis considered substitutes? Luckily, paragraphs 254 and 255 provide that distinctions between complements and substitutes are not clear cut, thus allowing certain levels of overlap between the concepts. Paragraph 254 states that if bundling partial substitutes results in efficiency benefits that the licensees might require, the technologies are treated as complements. Additional indications for efficiency include that individual licensing is allowed both by the participants and the pool in general, and the total royalties to all the individual licenses do not exceed the royalties charged by the pool.

It can be therefore be concluded that if synthetic biology matures into a properly modular technology, the creation of patent pools to facilitate downstream development is not *ex ante* prohibited. However, given the nature of partial substitutability, it would be wise for such pools to be constructed following the norms set out in paragraph 254 of the TTA Guidelines. It must also be noted that the TTA Guidelines contain a wealth of other provisions that are relevant to the formation of synthetic biology patent pools (paragraphs 244–273), but these matters cannot be addressed within the scope of this thesis.

6.1.3. Summation on the topic of market tools

Based on the discussion above, it is possible to state that the free market has somewhat sufficient means of managing potential fragmentation arising from the patenting of SynBio inventions, as well as mitigating overlap to some extent. The analysis has also shown that that free market tools have their limits. First of all, they may be incapable of solving certain collective action problems inherent in the creation of patent pools and clearinghouses. As

[461] van Passel et al 2014, p. 2–3.
[462] See e.g.: Quax et al. 2015, *passim*.

discussed in section 5.3., one possible solution for those problems is to enforce collective action through institutional means, which denotes either changes to patent policy, generating further incentives through e.g. fiscal incentives, or even passing entirely new legislation that mandates certain behavior. These measures will be addressed in the following chapter.

Despite the possible need to introduce institutional measures to fix incentive problems in the free market, it should be highlighted that the actors in the SynBio industry should take it upon themselves to further fix these issues. In this vein, Henkel and Reitzig put forth a convincing argument that the IP market actors themselves must understand the detrimental nature of abusing both the patent system and technology exchange regulations.[463] They advocate the following measures[464]: 1) high-technology firms should cease the construction of inflated patent portfolios, 2) firms must simplify standards and increase modularity of design, 3) innovators must begin cooperation in the early phase of their R&D processes, 4) companies must maintain a high level of interdepartmental and intercompany cooperation, and 5) stop unnecessary patenting altogether.[465]

Regardless of whether these incentive problems are fixed through institutional intervention or the SynBio patentees own volition, it is still necessary to formulate an ideal patent management structure that may serve as a goal for such efforts. As indicated by the discussion in the preceding sections of this chapter, both patent pools and clearinghouses have their benefits: patent pools may be efficient tools in managing horizontal fragmentation, although having a somewhat weaker effect in vertical fragmentation. Clearinghouses primarily engender benefits by reducing the transaction costs involved in downstream development, with some additional effects on vertical fragmentation. It is worth noting that the 2014 OECD SynBio Report advocates the creation of a synthetic biology clearinghouse that would register synthetic biology inventions, which could subsequently be licensed to users directly.[466] However, this model does not address horizontal fragmentation particularly well. In her study on both institutions, van Overwalle discusses the intriguing notion of combining both patent pools and clearinghouses into a *hybrid model*.[467] Especially

[463] Henkel & Reitzig 2008, para. 3.
[464] *N.B.:* The commentary is specifically geared towards minimizing the effects of PAEs, but given its general nature, it also pertains to all the issues discussed above.
[465] Henkel & Reitzig 2008, para. 15–19.
[466] OECD SynBio Report 2014, p. 103–104.
[467] Van Overwalle 2016, p. 22–23.

noteworthy is her comment on the MPP pool, which acts as a "type of 'supermarket' for a variety of disease related patents"[468].

Such a hybrid could potentially be the ideal model for synthetic biology as well, as it would have the potential to limit the effects of both horizontal and vertical fragmentation. One model that has seemingly not been considered at all in the literature is the notion of pooling multiple registries of bioparts and related technologies into separate patent pools, which could then centrally be administered through a clearinghouse. As an idealized example of this model, it is possible to imagine the following: patent pools A-D would be for proprietary biopart libraries, patent pool E would be for standard-essential patents, whereas patent pool F would be for patents on SynBio-specific research tools and other enabling technologies. The central clearinghouse, such as either a technology exchange or, ideally, a standardized license clearinghouse as in the OECD suggestions, would effectively connect these pools into a single resource, thus reducing the effects of both horizontal and vertical fragmentation. Such an arrangement would also reduce search costs, as a new developer would be able to search the clearinghouse to locate the necessary pooled patents quickly and efficiently. If the central clearinghouse is of the standardized license variety, the downstream developer would be able to obtain a license without having to engage in protracted negotiations. An additional benefit to this model is that it can be built incrementally through a primary stage of pooling the relevant patents, followed by the creation of the clearinghouse as a central institution connecting them all.

It is submitted that this would be the ideal free-market solution for the IP frame of synthetic biology, as it reduces both forms of fragmentation as well as reduces the effects of overlap, minimizing the potential of royalty stacking and patent hold-up, as well as reducing transaction costs considerably. As it arises naturally from the basic problem itself, it is surprising that it has not been suggested before now. However, its formation is contingent on solving the aforementioned problems inherent in patent pools. Furthermore, combining a standard license of modular optionality with the structure of a patent pool is by no means a simple proposition due to the aforementioned restrictions generated by EU competition law. Determining the feasibility of this model warrant further study in this respect.

[468] *Idem.* p. 23.

6.2. Patent policy tools

As indicated by the discussion above, the free market has the correct tools to create a functional SynBio IP model that addresses fragmentation, but possibly lack incentives to do so. If an economically functional combinatory model of patent pools and clearinghouses were constructed, institutional involvement would be necessary to solve the incentive problems inherent in patent pools and clearinghouses. Furthermore, relying solely on the free market to manage anticommons and patent thickets is unlikely to solve the fundamental issue of overlap.[469] This section seeks to cover both aspects of future patent policy.

6.2.1. Resolving patent overlap

As stated in several previous instances, resolving the patent overlap requires institutional action on part of the patent authority. One of the primary causes of overlapping patent claims is insufficient prior art research, both on the part of the applicant, as well as the patent authority themselves.[470] It is self-evident that applicants do not wish to expend any more resources in conducting such searches than absolutely necessary, but insufficient searches by the patent office are of greater concern. In his analysis on the matter, Lemley argues that patent offices are in fact "rationally ignorant" in not examining claims thoroughly, resulting in an overall lack of precise knowledge on the contents of prior art and existing patent claims.[471] It should however be noted that Lemley's criticisms were specifically directed towards the USPTO, although they are to some extent generalizable.

Prior art searches conducted by the EPO are generally accepted as being relatively good[472], but EPO Guideline B-III 2.1. contains an explicit acknowledgement that such measures are not always perfect. Even if a thorough search were to be conducted, there is always a chance that some *prima facie* unrelated patent contains-subject matter that overlaps with a patent application. In such situations, it is difficult for the authority themselves to notice potential overlap given the technical limitations of information search tools. This problem has both an *ex ante* and *ex post* solution; *ex ante* stricter interpretation of the criteria of patentability resulting in the narrowing of claims coupled with more thorough prior art searches, or *ex post* through post-grant opposition proceedings.[473]

[469] See: last paragraph of Section 4.3.1.
[470] Shapiro 2001, p. 125.
[471] Lemley 2001, *passim.*
[472] Chien & Kesan 2016, *passim.*
[473] Burk & Lemley 2003, p. 23.

Regarding the former, it must be stated that the EPO is not oblivious to the general cases of anticommons and patent thickets, with multiple studies conducted on how to best manage them. A 2012 EPO report suggests that managing patent overlap *ex ante* is one of the prime motives to increase overall patent quality.[474] The report agrees with Lemley's assessment in that increased prior art search costs lead to both overlapping claims in patent applications, as well as in difficulties for the examining board to notice the overlap in their prior art.[475] A similar 2013 EPO report identifies specific problems in the granting of European patents that promote the generation of patent thickets. Importantly, the report also offers some interrelated suggestions on how to fix these issues, granting high importance to improving the overall quality of patents, resulting in clearer boundaries between patents.[476] To this end, it also discusses further grant additional resources to examination to locate overlapping claims more efficiently[477], as well as means of reducing the total number of applications through a re-structuring of the costs of patent applications.[478] Overall, these measures will likely reduce not only overlap, but through effectively reducing the amount of patents granted, they will address fragmentation concerns as well. If implemented, they should provide a working *ex ante* solution for patent overlap.

The *ex post* opposition solution builds on Articles 99–103 of the EPC.[479] Article 99(1) provides anyone with the possibility to commence opposition proceedings up to nine months after the granting of the patent. EPC Article 100(a) provides that grounds for opposition include non-patentability of the subject-matter by virtue of it lacking one or more of the criteria of patentability contained in EPC Articles 52–57. As the question at hand is overlap, the most relevant criteria is *novelty*. Article 101 provides the actual remedies for successful opposition proceedings: revocation (Art. 101 (2.a)) or amending the patent (Art. 101 (3.a)). Article 99(2) provides that such remedies will have unitary effect in the contracting states in which the patent is in effect.

While undoubtedly a possibility, such opposition proceedings may prove to be economically problematic as a systemic solution. Thambisetty highlights the notion that in any

[474] EPO ESAB Report 2012, p. 7.
[475] *Idem.* p. 11.
[476] EPO ESAB Report 2013, p. 12.
[477] *Idem.*
[478] *Idem.*
[479] *N.B.:* Patent validity may also be questioned in other fora, but this discussion consciously omits those questions due to the implied increase of the role of national law, as well as the inherent spuriousness of speculation on UPC adjudication, as both would result in a topic too complex to discuss within the limited scope of this thesis.

adjudicative action that results in the invalidity of the patent, the subsequent invalidity of the patent is essentially a *public good*. The party seeking to invalidate the patent must bear the high costs of the invalidation process, with the other being able to freeride on the outcome.[480] In second, an unsuccessful attack on an existing patent may result in unfavorable outcomes, such as harsher licensing terms. As the cost of the royalties are likely passed at least partially to end consumers, this may result in higher prices and lower aggregate welfare.[481] To frame these conclusions in terms used previously: relying on free market actors to manage overlap in this manner results in a renewed collective action problem. Furthermore, solving that collective action problem is much more difficult than the version of solving fragmentation through patent pooling, as patent pooling results in a coherent bundle of *private property*, whereas an invalidated patent is a public good. There is no clear way for the opposing parties to appropriate the results of their efforts. The 2013 EPO report raises similar concerns, offering a multitude of possible solutions that include improving the opposition procedure, introducing better litigation systems, and better alternative dispute resolution.[482] However, the report itself indicates that effectuating all of the solutions discussed does not fall within the strict purview of the EPO[483], thus making it less likely that changes in EPO patent policy may provide a functional *ex ante* remedy to the problem of overlap.

In conclusion, it is clear that the simplest solution for managing any synthetic biology patent overlap in Europe must build upon institutional safeguards in the EPO patenting process itself. The measures suggested by the EPO seem sufficient, provided that they manage to maintain high standards of quality when faced with novel complex technologies, such as synthetic biology. In this vein, Robienski and Simon argue that it is unlikely that regulators will be especially challenged by the technical aspects specific to synthetic biology.[484]

6.2.2. Encouraging collective action

As discussed in sections 6.1.2–3, free market tools may mitigate fragmentation, but they suffer from a variety of incentive problems. The specific forms of incentive problem mentioned in that context were 1) 'market for lemons'-effect, 2) portfolio building, and 3) remaining outside the pool to extract holdup rents (generally referred to as *patent*

[480] Thambisetty 2013, p. 11.
[481] *Idem.* p. 12.
[482] EPO Report 2013, p. 12–14.
[483] *Idem.* p. 12.
[484] Robienski & Simon 2014, *passim.*

ambush)[485]. Given the systemic nature of these problems, it is difficult to see how the free market could resolve them independently. Scholars have suggested various forms of institutional intervention to ameliorate these problems.

First is the issue of the 'lemons market'. Van Zimmeren et al. have noted that this arises from a difficulty to obtain a critical mass of quality patents through voluntary participation of the patentees.[486] This implies that patentees might wish to benefit from a patent pool with a critical mass of valuable patents, but the coordination costs of the first movers may be too high. One possibility of resolving the issue would be to forcibly appropriate the patented technologies by means of compulsory licenses. Commentators have argued that that this approach is deeply problematic, as a trigger-happy policy of compulsory licensing may disincentivize innovation altogether.[487] One of the few legal scholars involved in synthetic biology that has addressed the issue of compulsory licensing is de Miguel Beriain, who argues that introducing compulsory licensing to manage potential obstruction in SynBio innovation "will definitely ruin any private investment in this market".[488]

A softer approach is possible. As evidenced by the participants in an EU-wide coordinated research effort on synthetic biology, ERASynBio, a great deal of synthetic biology research in Europe is conducted by publicly funded institutions, such as universities and national research academies.[489] As such institutions are not as reliant on market forces in their decision-making, it is possible for these institutions to take a policy stance of accruing their SynBio patents into a patent pool. Furthermore, public institutions may offer a credible *ex ante* commitment to maintain low royalty rates for such a pool, which Lévêque and Ménière argue will spur the growth of the pool even further.[490] In a similar vein, Carbone et al. argue that universities must take a more pro-active approach to disseminate the genetic technologies they have developed, as not doing so will easily lead to the exclusion of low-margin actors within an industry.[491]

Second is the portfolio issue. In their analysis, Weber and Parchomovsky present multiple solutions to the inflation of patent portfolios. Most noteworthy in this discussion are differential fees, in which patenting fees are partially determined by the size of the

[485] Hemphill 2005, p. 56–58.
[486] Van Zimmeren *et al.* 2011, 572.
[487] Verbeure 2009, p. 28.
[488] de Miguel Berian 2016, p. 147.
[489] ERASynBio Website, "About the ERASynBio Initiative".
[490] Lévêque & Ménière 2011, p. 244.
[491] Carbone *et al.* 2010, p. 788–791.

applicants' portfolio,[492] and increased disclosure requirements, which result in patents being granted only if they provide a sufficiently complete picture of the technology.[493] Very similar ideas were raised in the 2012[494] and 2013[495] EPO reports, which indicates that the EPO has at least considered such proposals. Given the similar nature of the questions, i.e. ensuring high quality patents, the portfolio issue may be addressed in conjunction with adopting the policies discussed in the previous section.

Patent ambush is a more complex issue, as it encroaches on the fundamental requirements of technology exchanges in the TTA Guidelines. Scholars have offered various solutions to this problem, with various degrees of potential. One such solution was presented by Klaus Schmidt, who recommends the following: if an essential technology is not included into the patent pool, the pool agreement is not valid.[496] This essentially means forcing a *grim* contingent strategy in solving the collective action problem. However, as stated previously, Axelrod has shown that such a solution is not optimal in terms of total welfare. Furthermore, it would be positively disastrous for synthetic biology patent pools, as it would be impossible to maintain such a level of essentiality given the potential for partial substitutability.

Other, less destructive measures exist. One commonly discussed option is the inclusion of so-called *grantback clauses* into the patent pool agreements, which generally denote an assurance on part of the either the participants or the licensees of the pool (or both) to license any upcoming essential technologies to the participants of the pool at FRAND terms.[497] This is a very effective tool in removing any incentive that a producing entity might have to hold out patents, as doing so would preclude them from participation in the pool altogether. The EPO 2013 report includes an additional suggestion to have some form of fiscal incentives for patentees that participate in patent pools.[498] It is likely that resolving potential patent ambushes will require a combined approach of specifically tailored incentives, which requires further economic modelling combined with empiric studies. Such studies are seemingly few and far between.

One last thing must be noted on this issue: not all patentees are necessarily producing entities. In the case of PAEs, who merely wish to extract royalties and consequently have no clear

[492] Weber and Parchomovsky 2005, p. 68–69.
[493] *Idem.* p. 69–71.
[494] EPO ESAB Report 2012, p. 16.
[495] EPO ESAB Report 2013, p. 12.
[496] Schmidt, K. 2010, p. 15–18.
[497] Merges 1999, p. 35–37.
[498] EPO ESAB Report 2013, p. 13

motivation to even participate in a patent pool, other measures are possibly required, such as compulsory licensing of PAE holdouts. Unfortunately, given the extreme complexity and fragmentation of the European compulsory licensing systems[499], they cannot be discussed further. It should be noted that since patent trolls rely fundamentally on injunctions to force the payment of high royalties[500], their effects can be mitigated through a rational structuring of the UPC. Further alleviating the problem is that European systems do not generally grant injunctions for infringing standard-essential patents unless the infringing party refuses to accept a FRAND license,[501] resulting in a marked decrease for the potential of PAEs to extract hold-up type rents by acquiring patents on fundamental SynBio infrastructure.

6.2.3. Managing PAEs

Robienski et al. note that while cross licensing, patent pools, and patent clearinghouses may certainly assist in reducing the problems of fragmentation and overlap, they are insufficient measures to provide an effective solutions. They highlight similar concerns as raised in previous sections of this thesis regarding the misaligned incentive structures of a) patent holders that engage in downstream development themselves and b) non-producing entities (the aforementioned 'patent trolls').[502] Following a similar logic leads Lemley and Shapiro to emphasize the strategic difficulty of getting non-producing entities to join in patent pools.[503] This discussion regarding managing the PAE problem will be divided into both this section and the subsequent one, with this one concentrating on more general issues, whereas the next one addresses the specific problem of PAEs in relation to patent pools.

One commonly raised concern pertains to the advent of the UPC, as it can conceivably provide patent trolls with a unified European forum to seek continent-wide injunctions and damages for the infringement of unitary patents.[504] UPCA Article 32(c) and (f) do theoretically provide this opportunity. Compounding the concerns relating to injunctions is the fact that the proposed UPC system follows the German model, in which injunctions can be granted prior to assessing whether the patent is even valid.[505]

[499] See: Tudor 2012, p. 230–238.
[500] Gabison 2015, p. 286–287.
[501] EC PAE Study 2016, p. 79.
[502] Robienski et al. 2016, p. 135.
[503] Lemley & Shapiro 2007, p. 2014.
[504] UKIPO UPC Study 2014, p. 26.
[505] EC PAE Study 2016, p. 42.

Several studies have been conducted that address this very question, often including comparisons of both the national court systems of Europe and the likely UPCA system with the respective patent infringement litigation procedures in the United States. Such studies tend to emphasize the fact that US patent trolls are generally considered to be a major problem in innovative industries[506], with as much as 60% of all patent litigation being generated by them.[507] One such study by Harhoff identifies several factors that have promoted deleterious PAE activity in the United States, the most important of which are high costs of legal action which are generally allocated to both parties, contingency fee payments for legal representation, high damage awards, a patentee friendly legal system, low quality of examination, extension of patent rights to subject-matter not considered patentable in Europe, and formerly, a high likelihood of obtaining an injunction if infringement was suspected.[508] However, empirical studies have shown that the situation is not as dire in Europe. A study by Helmers et al. shows that 11% of patent suits filed in the UK between 2000 and 2010 originated from non-producing entities[509], which is the hypernym that includes the aforementioned PAEs. The study does however show that such suits are most common in patents relating to high-tech inventions.[510]

What explains the marked difference between the US and Europe in the prevalence of PAEs? Harhoff shows that in regard to the aforementioned promoting effects, the European system is very dissimilar to the US one, most importantly in that the loser generally bears the costs of litigation, and European systems generally do not contain so-called treble damages.[511] An extensive study conducted under the auspices of the European Commission alleviates these fears further by stating *inter alia* that the European patent system manages patent quality better than the US system, and European courts tend to be overall more critical of injunctive measures. Furthermore, seeking unitary injunctions carries the risk of exposing the potential invalidity of the patent, and the European "loser pays"-system is likely to disincentivize patent trolls altogether.[512] The study does conclude that PAEs will likely be active

[506] Henkel & Reitzig 2008, *passim.*
[507] Gerardin 2016, p. 2.
[508] Harhoff 2009, p. 49.
[509] Helmers *et al.* 2014, p. 509.
[510] *Idem.*, p. 534, Table 2.
[511] Harhoff 2009, p. 50.
[512] EC PAE Study 2016, p. 42–44.

immediately after the creation of the UPC to test the system, but they will find it difficult to adapt their business models to fit the European standards.[513]

Based on the discussion above, it can be concluded that the advent of the UPC will likely have little effect in the way of fostering patentee behavior that is detrimental to the development of synthetic biology. Given the relatively minor role that patent trolls have played in the European patent landscape, their effect on European SynBio innovation is likely to be minimal, thus alleviating the concerns of scholars such as Robienski. As stated in the EC report, this is naturally contingent on the UPC adopting sufficiently stringent criteria when evaluating issues such as the granting of temporary injunctions.[514] The UPC organization seems to be well aware of such concerns, even addressing them on their website.[515] An interesting question in this respect is whether the UPC will adopt the jurisprudence of the ECJ on the intellectual property related provisions of TJEU Articles 101 and 102, which together have been used as a means for putative infringers to argue against abusive licensing practices regarding patents that confer market dominance.[516] However, that is a question for another study.

6.3. Considerations de lege ferenda

Evaluating the conclusions of the chapter so far leads to the conclusion that neither free market actors nor patent policymakers will likely find the current framework of IP legislation and competition law insufficient in dealing with the challenges posed synthetic biology. Even if the legislative frame is largely sufficient in ensuring the viability of synthetic biology, doing so in practice requires that both the developers of synthetic biology as well as the institutions charged with managing patent policy take action in effectuating the recommendations described above.

There is however one issue that has been discussed in this work which is not sufficiently addressed by current legislation. Referring back to section 4.4., if bioparts become truly standardized and modular, the 'reasonable expectation of success' doctrine of the EPO may prove problematic for the developers of downstream applications of synthetic biology.

[513] *Idem.* p. 44.
[514] *Idem.* p. 42–43.
[515] UPC Website FAQ, under "Will the UPC make it easier for non-practicing entities (patent trolls) to sue innovative companies?".
[516] See *e.g.*: Gerardin 2016, p. 11–24 for a thorough analysis on the utilization of TFEU Articles 101 and 102 in this manner.

Because of the entrenched position of this doctrine in EPO law and its importance for issues outside synthetic biology, any *de lege ferenda* suggestion to modify the standard, if one were to be implemented, would likely to result in far-reaching and unpredictable outcomes. As this thesis aims for simple solutions that do not disrupt the current patent system excessively, an alternative method of resolving the issue is needed.

6.3.1. Harmonized utility model protection

A natural candidate for resolving the issue is *utility model* (UM) protection. Utility models are a means to obtain IP protection for inventions that fall short of the strict subject-matter criteria inherent in the European patent system.[517] UMs are broadly similar to patents in that most European countries utilize similar subject-matter criteria for both utility models and patents, but only consider some of those criteria, or use lower standards in evaluating them.[518] As an example, while novelty is a criterion for obtaining a UM, this requirement is not necessarily absolute. Depending on the European nation in question, utility models may require absolute novelty, such as provided in section 2 of the Finnish Utility Model Act.[519] As a counterexample, Article 145.1 of the Spanish Patent Act[520] states that novelty is assessed based on prior disclosure in Spain alone. The greatest difference between utility models and patents is that the former are generally not examined by the granting authority.[521] In evaluating the aforementioned criteria, the granting authority relies primarily on disclosure by the applicant. The overall ease of obtaining utility models is compensated by the fact that the period of protection they offer is usually considerably shorter than that of patents[522], with between seven to ten years being the most common period.[523]

As utility models are easier to obtain and generally cost less, Minssen et al. have suggested that a harmonized European approach in utility model protection would generally promote innovation in European synthetic biology, as small-to-medium enterprises (SMEs) would be able to obtain protections for their innovations for relatively low costs. [524]

A shared form of utility model protection arising from EU legislation would have the benefit of offering a partial solution to the issue arising from the 'reasonable expectation of success'

[517] Sutheransen & Dutfield 2007, p. 18.
[518] *Idem.* p. 25–30.
[519] Laki hyödyllisyysmallioikeudesta (10.5.1991/800)
[520] Ley 11/1986, de 20 de marzo, de Patentes.
[521] Sutheransen & Dutfield 2007, p. 14.
[522] Burk 2016, p. 25.
[523] WIPO IP for Business webpage.
[524] Minssen et al. 2015, p. 239, under "Recommendation 6"

doctrine in EPO patent law, as the EPO does not concern itself with utility models. This would provide downstream SynBio innovators with the necessary incentives to develop even quite simple commercial applications by allowing them to recoup their development and licensing costs. This would also be acceptable in terms of the general logic of IPR protection by acknowledging the fact that a relatively straightforward assembling of bioparts is not innovative enough to warrant 20 years of exclusivity through traditional patent protection. A *harmonized* UM framework is also required by the fact that Member states that have adopted UM legislation have generally included very different approaches regarding biotechnological inventions. As an example, section 6(1.2) of the Estonian Utility Model Act provides that biotechnological inventions may not be granted UM s.

It should be noted that the European Commission proposed a directive harmonization of utility model protection in 1997, which was subsequently updated in 1999. This approach was suspended in the year 2000 and finally abandoned in 2006 due to lack of consensus.[525] It may be the opportune time to revisit the matter. As it currently stands, the specific case of synthetic biology by itself is likely insufficient to warrant renewed harmonization efforts for utility model protection. Nonetheless, it does serve as a compelling example of one of many complex technologies that would benefit from such harmonization. The primary message and *de lege ferenda* proposal arising from this particular discussion is that biotechnological inventions should be included within the scope of any future utility model protection.

It is necessary to include one caveat: given the general ease of obtaining a UM, great care must be taken that granting them to minor inventions in synthetic biology does not create a *utility model anticommons and thicket* on top of what was previously discussed in regards to patenting. While in no way relating to the European development of synthetic biology, commentators have discussed the emergence of such utility model thickets in China[526], indicating that they are at least a conceptual possibility. One quite invasive way to solve the problem would be to include a provision in the prospective directive that requires FRAND licensing of all utility modes.

[525]EC Growth SME Website: Utility Models
[526] Luginbuehl 2014, p. 16–17.

7. Concluding remarks

As outlined in the introduction of this thesis, its purpose was to study the compatibility of synthetic biology with existing European patent law, especially with regards to the latter's capability of generating efficient solutions that would ensure the viability of the technology. While attempting to address this problem, this work wound up covering multiple issues that have not been discussed by scholars of the field so far, except for analogous situations in the precursors of synthetic biology. The implications of the substantive rules of patentability of the EPC on the development of synthetic biology have been discussed in other work, but usually focusing on a very specific issue. Second is an approach that builds on empirical similarities between synthetic biology and its precursors. Third is a more thorough analysis of the market tools for addressing fragmentation and overlap as they relate specifically to synthetic biology. Fourth is the implications of European competition law on the viability of those market tools. To my knowledge, the last issue has remained totally in the dark so far. While researching these issues, an extremely broad field of inquiry revealed itself, one which hopefully will be populated by researchers more qualified than I. However, in order to give a proper closure to this work, it is suitable to conclude by answering the research questions outlined in the very beginning.

Why is synthetic biology a special case? Synthetic biology has the potential to revolutionize our everyday lives by bringing true engineering principles to genetic engineering. In that pursuit, it will also adopt characteristics of fields that are not normally associated with biotechnology, such as electrical engineering and computing. The modular approach discussed in this work is of especially high relevance to all legal professionals and institutions, as it poses difficult questions in fields of private law, such as IP law, but also in bioethics, biosafety, and biosecurity. Multiple institutional actors have realized what is just over the horizon and have begun to adapt their regulations and policies to adapt. One very characteristic quality of synthetic biology is its commitment to keeping knowledge accessible, similar to how the open source ethos of Linux has taken shape over the past few decades. It is my hope that this area of free innovation will exist long into the future, and learn to co-exist with its more traditional sibling, the IP frame.

How does synthetic biology relate to European patent law? In respect to patent law, the most natural way to view synthetic biology is as mostly an extension of pre-existing forms of biotechnology. The definitions contained by the Biotechnology Directive make it abundantly

clear that the European regulator will consider synthetic biology as such. As for the EPO, the question is more multifaceted. Given the EPC's unshakeable dogma of technology neutrality, various existing jurisprudential solutions may have the potential to engender unintended consequences. This thesis contained only a minuscule sample of pertinent cases, meaning that follow-up research is definitely warranted to provide a more coherent picture of EPO jurisprudence in relation to synthetic biology. However, by and large, it would seem that Robienski & Simon are correct in stating that the novelty factor of synthetic biology as currently exists may be somewhat overstated[527], as this work did not result in any conclusions that would necessitate a paradigm shift in patent protection. This is naturally subject to ongoing change.

Patent fragmentation and overlap/transaction costs. The major problems that will quite likely become the bane of SynBio downstream developers' existence are the tragedy of the anticommons and patent thickets. These issues are not unique to synthetic biology, but given the ever-increasing role they have to play in established fields of technology, they pose a severe threat to a nascent one. It is likely that developers will be faced with decreasing freedom to operate, unless both market actors, governmental institutions and an effective framework of governing SynBio IP. The compounded risks of high transaction costs and double-marginalization are difficult to overcome, but solutions do exist. The model developed in section 6.1.4. is an ideal that should be strived towards, as it provides the maximal reduction to fragmentation and transaction costs.

Collective action. Building the model described above is likely to be a complicated proposition. Given the high levels of potential patent subject-matter inherent in developing novel organisms through the bioparts approach, it is difficult to align the interests of all relevant actors in the field. Both this and solving the overlap problem require institutional measures, both on the part of patent authorities, as well as publicly funded research institutions. The former must strive to increase patent quality by utilizing whatever means they have. If successful, such measures will likely ameliorate the underlying problem considerably. Universities and national research councils should take a proactive approach in shaping the future IP landscape, lest they become the victims of it. Furthermore, the UPC should adopt a pro-innovative approach in dealing with IP actors that merely seek to benefit from the detriment of others by extracting rents. So far, these patent trolls are not a

[527] Robienski & Simon 2014, p. 123.

considerable problem in Europe, but if mismanaged, they may potentially become as detrimental a force in Europe as they currently are in the United States. One final caveat is issued in this respect: it might be difficult to distinguish between an innovation-generating pool and a collection of predatory patent trolls. As indicated above, this thesis was by no means a conclusive study on these issues. Further study on all of these question is definitely mandated, both because of the limited scope of this thesis, as well as the need to develop and modify the framework further

In summation, it is hoped that this work will generate some modicum of interest in synthetic biology, be it scholarly or non-academic, focusing on the IP issues or the technology itself. As an effective layman, albeit a highly avid one, in questions related to molecular biology and normative economics, I certainly will follow the development of synthetic biology with a high level of interest. Given its promise, it may be the third milestone in our species mastery of biology. Perhaps it will even result in the predictions made by the participants in Calvert and Frow's study becoming true, and we will have "tortoises that are also TV screens, and mini fighting dinosaurs"[528]. It just might be that creating novel organisms through the tools provided by synthetic biology will satisfy Feynman as well.

[528] Frow & Calvert 2013, p. 37.

Appendix 1

Background concepts and definitions for economic analysis

I. Rational choice theory

As stated in the methodology section, this thesis relies heavily on a law and economics approach. As with most forms of economics, it is based on an assumption of rationality of the relevant economic actors, which is also known as *rational choice theory.*[529] This theory is in itself is contentious, meaning that an invoking an economic approach without discussing the rationality assumption would render the conclusions of this thesis questionable. The aim of this discussion is to formulate a rigorous rational choice theory that will serve as the theoretical cornerstone of the economic thought demonstrated in the thesis proper.

The genesis of rational choice theory lies within Richard Posner's seminal book, *Economic Analysis of Law*[530]. Posner formulated certain fundamental concepts that underlie his approach in law and economics. These concepts are contingent on his formulation of the assumption of rationality, which he posits as follows: "[M]an is a rational maximizer of his ends in life, his satisfactions — what we shall call his 'self-interest.'"[531]. This notion of was criticized almost immediately. In one such influential critique, Arthur Allen Leff argues that the supposed empirical and scientific underpinnings of Posner's rational choice theory were neither empirically formulated, nor were they even empirically verifiable.[532]

In the intervening decades, other scholars created other forms of the assumption. Korobkin and Ulen sought to categorize these various forms of rational choice theory by placing them on a spectrum, ranging from "thin" to "thick" conceptions, with thinner versions being less scientifically rigorous and thick ones being more so. According to their critique, Posner's definitional formulation is the thinnest of them all by virtue of providing no testable predictions, not delineating the scope of rationality (i.e. all behavior can be ex post described as rational) and being entirely non-falsifiable.[533] The thickest form of rationality is one which

[529] *N.B.:* the terms 'rationality assumption' and 'rational choice theory' are used interchangeably in this text.
[530] *N.B.:* the first edition of *Economic Analysis of Law* was published in 1973
[531] Posner 2002, p. 3
[532] See e.g. Leff 1974, p. 456–457, in which
[533] Korobkin & Ulen 2000, p. 1061–1062.

posits that actors seek to maximize their monetary and financial gains.[534] Thick forms of the rational choice theorem are more rigorous in the sense that they make testable predictions, being clear in their scope and creating a clear criterion of falsifiability.[535] If the economic actor acts in a way that does not maximize their short or long-term financial gains, the rationality assumption is falsified.

A dialectic approach to rational choice theory and its criticism leaves us with a candidate for synthesis: limited liability companies. This choice is in part validated by legislation. As an example, Chapter 1, Section 5 of the Finnish Limited Liability Company Act (21.7.2006/624) provides that the purpose of the company is to generate profits to its shareholders, unless otherwise provided in the Articles of Association. This brings the purpose of a limited liability company very close to the thick form of rational choice theory. This leaves us with the empirical truth of the matter: do limited liability companies act this way? The traditional, Schumpeterian answer to this is that companies that fail to do so are eliminated through a market-generated Darwinian selection process.[536] Other commentators have pointed out that groups of people, as generally found in companies, generally perform better on tasks measuring rational choice.[537] However, commentators such as Langevoort have noted that managerial rationality in organizations is more of an ideal than an empirical truth, as lucrative IPRs can lead to a competency trap in which the competitive element of the free market is unable to ensure rational behavior.[538] This question remains somewhat open, but it does not mean that a rational approach is without merit. Creating a framework based on the thick form of rational choice theory allows for SynBio companies themselves to adopt an IPR strategy that maximizes their utility. This changes the underlying form of rational choice theory to be a *prescriptive* claim on how synthetic biology IPR holders ought to act, instead of a *descriptive* claim on how they actually behave.

It is now possible to formulate a rational choice theory that takes into account all of the above and which will serve as the basis of the economic analysis contained within this thesis:

1) The holders of synthetic biology IPRs are generally speaking limited liability companies.

[534] Korobkin & Ulen 2000, p. 1066.
[535] *Idem.*
[536] Magnusson 1994, p. 2–4.
[537] Kugler et al. 2012, *passim.*
[538] Langevoort 2000, p. 154

2) The relevant companies seek to maximize their financial gains (thick form of rational choice theory).
3) It is not possible to determine whether the relevant companies act in full accordance to rational choice theory in managing their IPRs.
4) It is in the interest of the companies themselves that they should act in accordance to rational choice theory, and they are capable of doing so in the limited question of IPR management.

By adopting the wealth maximization version of the rationality assumption in this thesis, the results and suggestions contained herein can be falsified at least in part by providing empirical evidence that contradicts the assumptions above. In other words, if actors in the synthetic biology IPR landscape do not even intend to maximize their gains in a rational manner, the conclusions of this thesis can be considered suspect.

II. Efficiency

As stated in the introduction, the aim of the thesis proper is to create an efficient framework for synthetic biology IPR management that ensures the viability of the technology. What exactly does efficiency mean in this context? Unfortunately, there is no simple answer, as there are multiple forms of efficiency that must be considered together. In analyzing the incentives of innovation, Motta distinguishes between two forms of efficiency: *ex ante* efficiency and *ex post* efficiency. The former is characteristic of a regulatory system that seeks to incentivize firms to innovate and develop the market further, whereas the latter is concerned with the notion that, when an invention has been developed, it would be optimal for all relevant firms in the market to be able to utilize it freely, creating increased welfare through increased competition.[539] Motta's concepts are applications of the general economic concepts of dynamic and static efficiency[540] respectively.

Static and dynamic efficiency cannot be maximized simultaneously, as there is an inherent trade-off between the two. Optimizing static efficiency leads to lower prices in the short run, whereas optimizing dynamic efficiency leads to somewhat higher prices, but with the potential for innovations that increase overall efficiency in the future.[541] It is easy to note the conflicting aims of these forms of efficiency in relation to IP policy. If one seeks to optimize

[539] Motta 2004, p. 65.
[540] *N.B.:* Static efficiency itself is a hypernym for various forms of efficiency, the most important of which are *allocative efficiency* and *productive efficiency*. For a further discussion on the specifics of these forms of efficiency, see e.g.: Kathuria 2015, p. 321.
[541] Kathuria 2015, p. 319–320.

static efficiency, such as by not offering any form of IPRs protection, it reduces the innovator's market power, which Motta argues is the primary incentive to engage in R&D.[542] This freeloading on other's R&D in turn means that dynamic efficiency is greatly reduced, as innovators are unable to recoup their costs. This is of considerable concern. As Blaug points out, from a historic perspective, dynamic efficiency has had a greater positive impact on welfare than optimal static efficiency.[543] Conversely, if the legislator would seek to optimize dynamic efficiency by offering expansive IPR protection, such as overly broad patent scope and length, it would easily result in the formation of monopolies.[544] Monopolies are welfare detrimental both in terms of static and dynamic efficiency, as they are able to charge monopoly prices[545] and have a lesser need to engage in further innovation to protect their market power[546].

As the purpose of this thesis proper is to ensure the viability and development of synthetic biology as a field, it is necessary to concentrate more on questions of dynamic efficiency. This is also justified in relation to the rationality choice theorem adopted in this thesis, as scholars of corporate economic strategy have emphasized the importance of dynamic efficiency in increasing market power, although reminding us that it would be erroneous to consider panacea in terms of corporate strategy.[547] As the ultimate purpose is to ensure welfare, this approach is also justified by the notions presented by Motta. However, static efficiency creates a boundary for normative suggestions made in the name of dynamic efficiency.

[542] Motta 2004, p. 64.
[543] Blaug 2001, p. 44–45.
[544] Motta 2004, p. 56.
[545] For an analysis of the static inefficiency of monopolies, see: Viscusi et al. 2005, pp. 80–84.
[546] Tirole 1998, p. 392
[547] Ghemawat & Ricart I Costa 1993, p. 72.